

Fig.1.

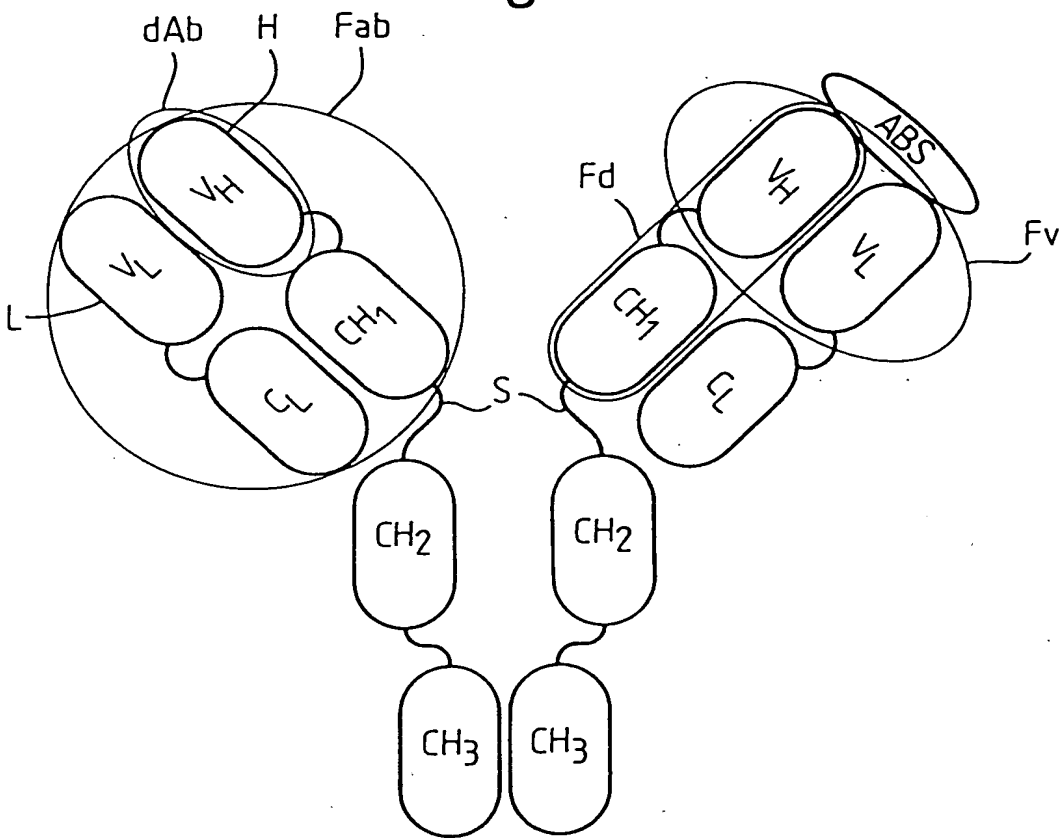


Fig.2 a

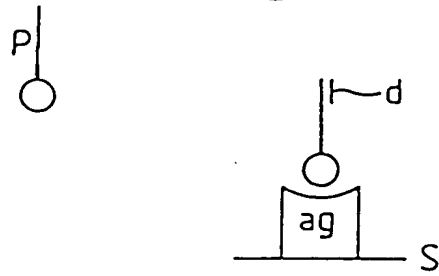


Fig.2 b

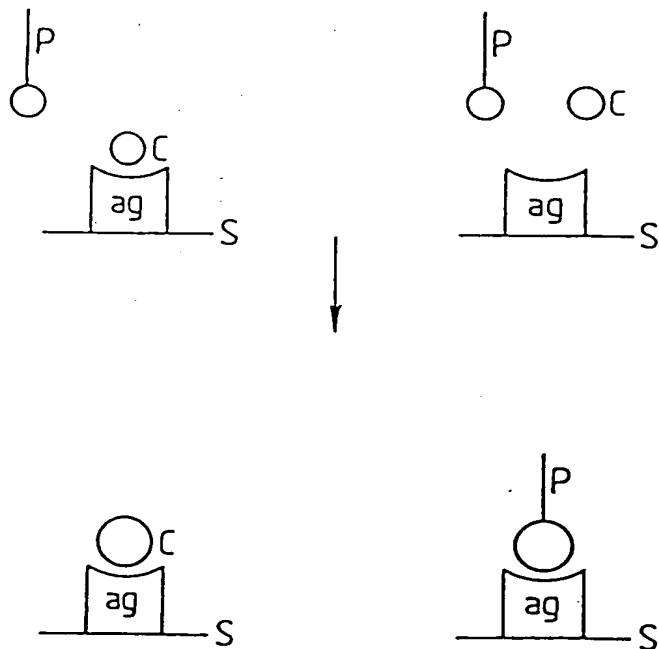
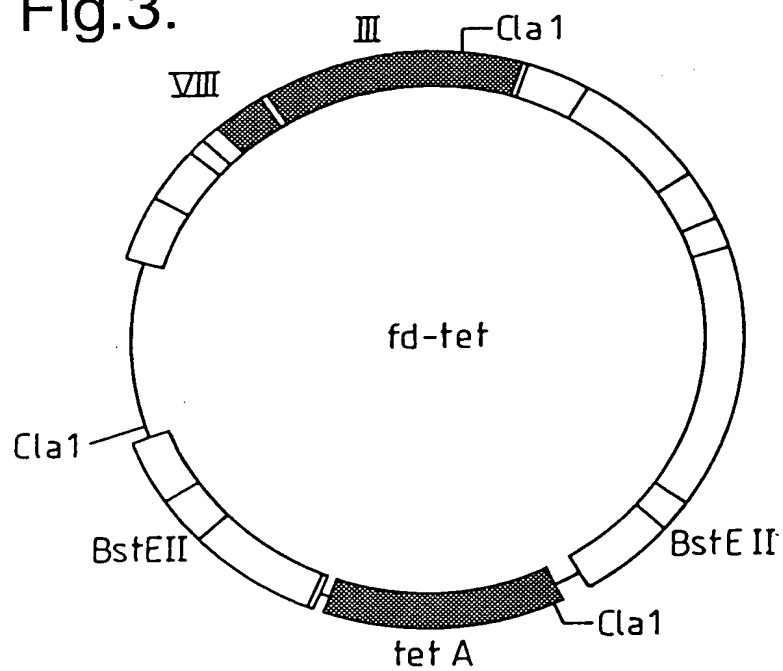


Fig.3.



fd - tet
~
cleave with BstEII
~
fill in with Klenow
~
re-ligate
↓
FDTδBst
~
in vitro mutagenesis (oligo 1)
↓
FOTPs/Bs
~
in vitro mutagenesis (oligo 2)
↓
FOTPs/Xh

Fig.5a

rbs M K Y L L P T A A
 GCATGCAAATTCTATTTCAAGGAGACAGTCATAATGAAATACCTATTGCCTACGGCAGCC
 10 20 30 40 50 60
 SphI
 PelB leader
 A G L L L L A A O P A M A Q V Q L Q E S
 GCTGGATTGTTATTACTCGCTGCCCAACCAGCGATGGCCCAGGTGCAGCTGCAGGAGTCA
 70 80 90 100 110 120
 PstI
 G P G L V A P S Q S L S I T C T V S G F
 GGACCTGGCCTGGTGGCGCCCTCACAGAGCCTGTCCATCACATGCACCGTCTCAGGGTTC
 130 140 150 160 170 180
 S L T G Y G V N W V R Q P P G K G L E W
 TCATTAACCGGCTATGGTGTAAACTGGGTTCCGCCAGCCTCCAGGAAAGGGTCTGGAGTGG
 190 200 210 220 230 240
 VHD1.3
 L G M I W G D G N T D Y N S A L K S R L
 CTGGGAATGATTTGGGGTGATGGAAACACAGACTATAATTCAGCTCTCAAATCCAGACTG
 250 260 270 280 290 300
 S I S K D N S K S Q V F L K M N S L H T
 AGCATCAGCAAGGACAACCTCCAAGAGCCAAGTTTTCTTAAAAATGAACAGTCTGCACACT
 310 320 330 340 350 360
 D D T A R Y Y C A R E R D Y R L D Y W G
 GATGACACAGCCAGGTACTACTGTGCCAGAGAGAGAGATTATAGGCTTGACTACTGGGGC
 370 380 390 400 410 420
 Linker Peptide
 Q G T T V T V S S G G G G S G G G G S G
 CAAGGCACCAACGGTCAACCGTCTCCTCaggtggagggcggttcaggcgaggtggctcgggc
 430 440 450 460 470 480
 BstEII
 G G G S D I E L T Q S P A S L S A S V G
 ggtggcggatcgGACATCGAGCTCACTCAGTCTCCAGCCTCCCTTTCTGCGTCTGTGGGA
 490 500 510 520 530 540
 SacI

Fig.5 b

E T V T I T C R A S G N I H N Y L A W Y
GAAACTGTCACCATCACATGTCGAGCAAGTGGGAATATTACAAATTATTTAGCATGGTAT
550 560 570 580 590 600

Q Q K Q G K S P Q L L V Y Y T T T L A D
CAGCAGAAACAGGGAAAATCTCCTCAGCTCCTGGTCTATTATACAAACCTTAGCAGAT
610 620 630 640 650 660

VKD1.3

G V P S R F S G S G S G T Q Y S L K I N
GGTGTGCCATCAAGGTTTCAGTGGCAGTGGATCAGGAACACAATATTCTCTCAAGATCAAC
670 680 690 700 710 720

S L Q P E D F G S Y Y C Q H F W S T P R
AGCCTGCAACCTGAAGATTTTGGGAGTTATTACTGTCAACATTTTGGAGTACTCCTCGG
730 740 750 760 770 780

Myc Tag (TAG1)

T F G G G T K L E I K R E O K L I S E E
ACGTTTCGGTGGAGGGACCAAGCTCGAGATCAAACGGGAACAAAACTCATCTCAGAAGAG
790 800 810 820 830 840

XhoI

D L N * * (SEQ ID NO. 183)

GATCTGAATTAATAATGATCAAACGGTAATAAGGATCCAGCTCGAATTC (SEQ ID NO. 184)
850 860 870 880

EcoRI

Fig.6.

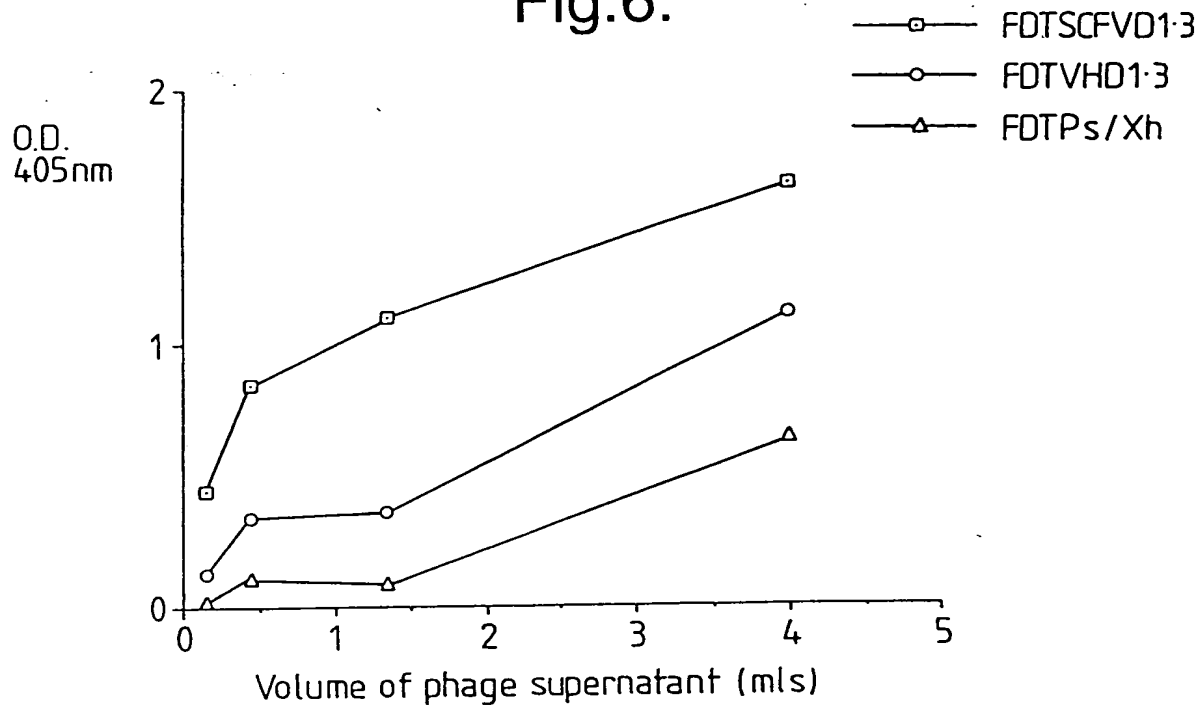


Fig.7.

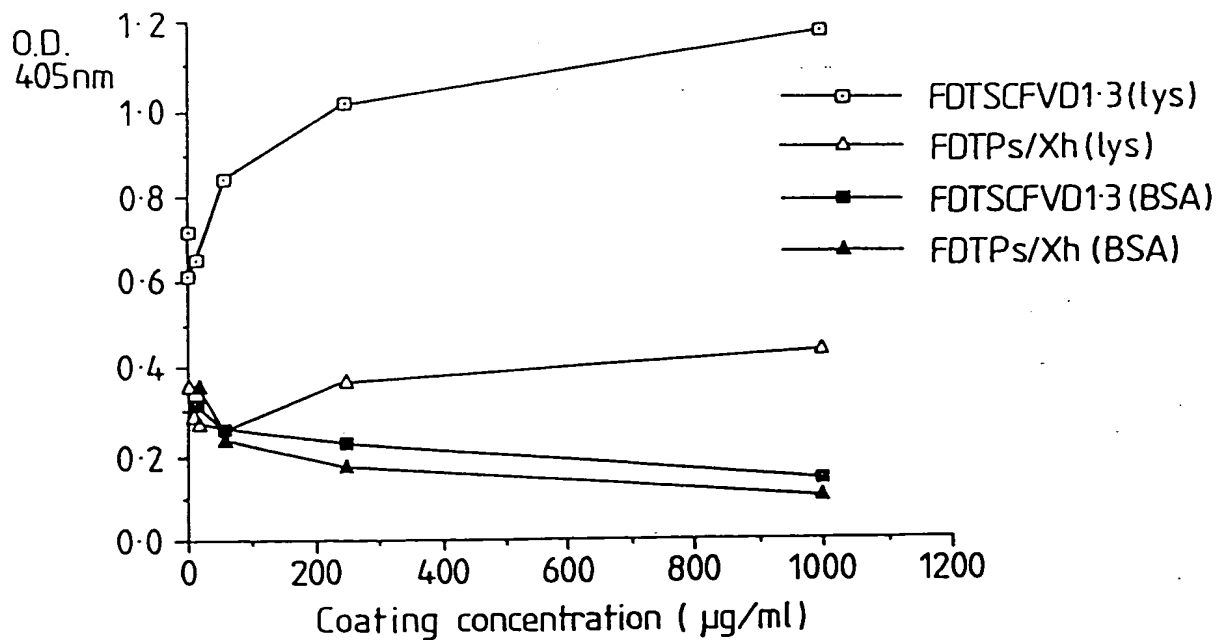


Fig.9.

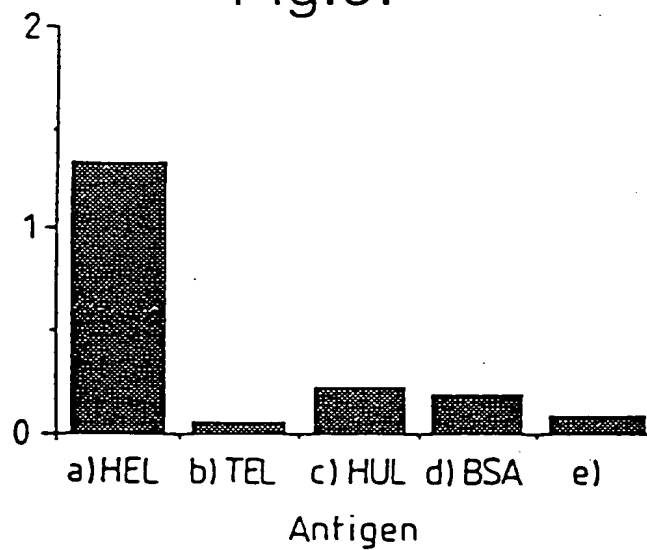
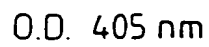


Fig.10a

M K Y L L P T A A
GCATGCAAATTCTATTTCAAGGAGACAGTCATAATGAAATACCTATTGCCTAGGGCAGCC
10 20 30 40 50 60

A G L L L L A A Q P A M A Q V Q L Q E S
GCTGGATTGTTATTACTGCTGCCCCAACCAGCGATGGCCCTGGTGCAGCTGCAGGAGTCA
70 80 90 100 110 120

G P G L V A P S Q S L S I T C T V S G F
GGACCTGGCCCTGGTGGCGCCCTCACAGAGCCTGTCCATCACATGCACCGTCTCAGGGTTC
130 140 150 160 170 180

S L T G Y G V N W V R Q P P G K G L E W
TCATTAACCGGCTATGGTGTAAACTGGGTTCCGCCAGCCTCCAGGAAAGGGTCTGGAGTGG
190 200 210 220 230 240

L G M I W G D G N T D Y N S A L K S R L
CTGGGAATGATTGTTGGGGTGATGGAAACACAGACTATAATTCAGCTCTCAAATCCAGACTG
250 260 270 280 290 300

S I S K D N S K S Q V F L K M N S L H T
AGCATCAGCAAGGACAACCTCCAAGAGCCAAGTTTTCTTAAAAATGAACAGTCTGCACACT
310 320 330 340 350 360

D D T A R Y Y C A R E R D Y R L D Y W G
GATGACACAGCCAGGTACTACTGTGCCAGAGAGAGAGATTATAGGCTTGACTACTGGGGC
370 380 390 400 410 420

Q G T T V T V S S A S T K G P S V F P L
CAAGGCACCAAGGTCAACGTCTCCTCAGCCTCCACCAAGGGCCCATCGGTCTTCCCCCTG
430 440 450 460 470 480

A P S S K S T S G G T A A L G C L V K D
GCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGGGCCCTGGGCTGCCTGGTCAAGGAC
490 500 510 520 530 540

Fig.10b

Y F P E P V T V S W N S G A L T S G V H
TACTTCCCCGAACCGGTGACGGTGTCTGTGGAACCTCAGGCGCCCTGACCCAGCGGGGTGTCAC
550 560 570 580 590 600

T F P A V L Q S S G L Y S L S S V V T V
ACCTTCCCCGGCTGTCTTACAGTCTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTG
610 620 630 640 650 660

P S S S L G T Q T Y I C N V N H K P S N
CCCTCCAGCAGCTTGGGCAACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAAC
670 680 690 700 710 720

T K V D K K V E P K S S * * (SEQ ID NO. 187)
ACCAAGGTGACACAAGAAAGTTGAGCCCCAAATCTTCATAATAACCCGGGAGCTTGCATGCA
730 740 750 760 770 780

M K Y L L P T A A A G L
AATTCTATTTCAGGAGACAGTTCATAATGAAATACCTATTGCGCTACGGCAGCCGCTGGAT
790 800 810 820 830 840

L L L A A Q P A M A D I E L T Q S P A S
TGTTATTACTCGCTGCCCCAACCCAGCGATGGCCGACATCGAGCTCACCAGTCTCCAGCCT
850 860 870 880 890 900

L S A S V G E T V T I T C R A S G N I H
CCCTTCTGCGTCTGTGGGAGAACTGTACCATCACATGTGCGAGCAAGTGGGAATATT
910 920 930 940 950 960

N Y L A W Y Q Q K Q G K S P Q L L V Y Y
ACAATTATTTAGCATGGTATCAGCAGAAACAGGGAAATCTCCTCAGCTCCTGGTCTATT
970 980 990 1000 1010 1020

Fig.10 c

T T T L A D G V P S R F S G S G S G T Q
ATACAACAACCTTAGCAGATGGTGTGCCATCAAGGTTTCAGTGGCAGTGGATCAGGAACAC
1030 1040 1050 1060 1070 1080

Y S L K I N S L Q P E D F G S Y Y C Q H
AATATTCTCTCAAGATCAACAGCCTGCAGCCTGAAGATTTTGGGAGTTATTACTGTCAAC
1090 1100 1110 1120 1130 1140

F W S T P R T F G G G T K L E I K R T V
ATTTTGGGAGTACTCTCGGACGTTGGGTGGAGGCCACCAAGCTCGAGATCAAACGGACTG
1150 1160 1170 1180 1190 1200

A A P S V F I F P P S D E Q L K S G T A
TGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAAGT
1210 1220 1230 1240 1250 1260

S V V C L L N N F Y P R E A K V Q W K V
CCTCTGTGTGTGTGCTGCTGAATACTTCTATCCCAGAGAGGCCAAAGTACAGTGGGAAGG
1270 1280 1290 1300 1310 1320

D N A L Q S G N S Q E S V T E Q D S K D
TGGATAACGGCCCTCCCAATGGGGTAACTCCCAGGAGTGTACAGAGCAGGACAGCAAGG
1330 1340 1350 1360 1370 1380

S T Y S L S S T L T L S K A D Y E K H K
ACAGCACCTACAGCCTCAGCAGCAACCTGACGCTGAGCAAAGCAGACTACGAGAAACACA
1390 1400 1410 1420 1430 1440

V Y A C E V T H Q G L S S P V T K S F N
AAGTCTACGCTGCGAAGTCAACCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCA
1450 1460 1470 1480 1490 1500

R G E S * * (SEQ ID NO. 188)
ACCGGGAGAGTCATAGTAAGAATTC (SEQ ID NO. 189)
1510 1520

Fig.10 d

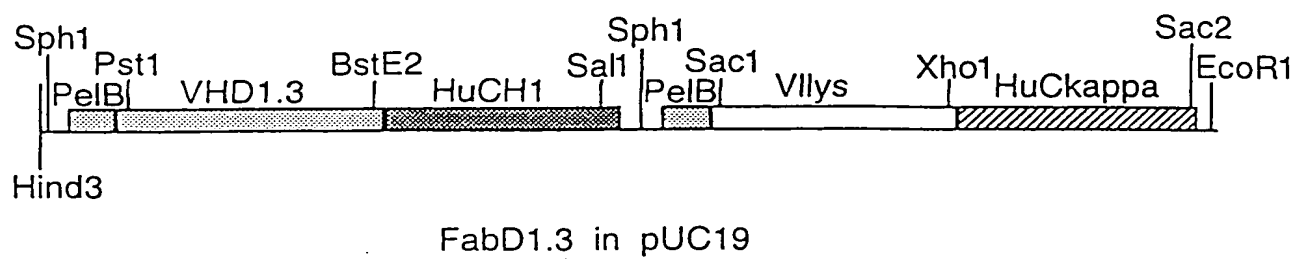


Fig.11.

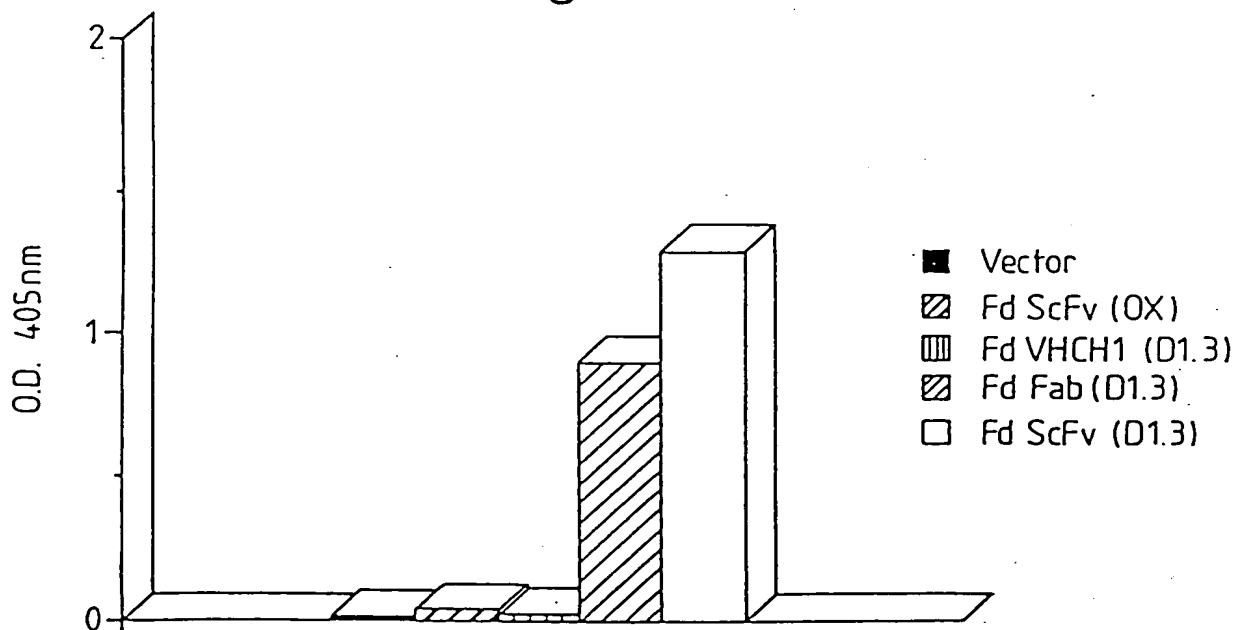


Fig.12a.

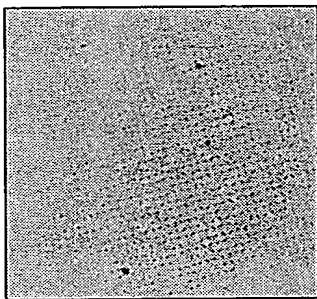


Fig.12b.

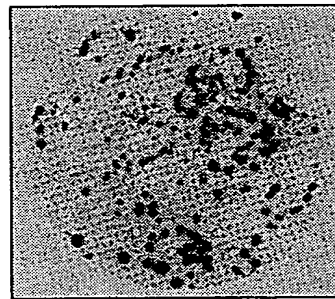


Fig.13.

Q V Q L Q E S G G G L V Q P G G
 CAG GTG CAG CTG CAG GAG TCA GGA GGA GGC TTG GTA CAG CCT GGG GGT
 PstI
 S L R L S C A T S G F T F S N Y
 TCT CTG AGA CTC TCC TGT GCA ACT TCT GGG TTC ACC TTC AGT AAT TAC
 Y M G W V R Q P P G K A L E W L
 TAC ATG GGC TGG GTC CGC CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG
 G S V R N K V N G Y T T E Y S A
 GGT TCT GTT AGA AAC AAA GTT AAT GGT TAC ACA ACA GAG TAC AGT GCA
 S V K G R F T I S R D N F Q S I
 TCT GTG AAG GGG CGG TTC ACC ATC TCC AGA GAT AAT TTC CAA AGC ATC
 L Y L Q I N T L R T E D S A T Y
 CTC TAT CTT CAA ATA AAC ACC CTG AGA ACT GAG GAC AGT GCC ACT TAT
 Y C A R G Y D Y G A W F A Y W G
 TAC TGT GCA AGA GGC TAT GAT TAC GGG GCC TGG TTT GCT TAC TGG GGC
 Q G T L V T v s s g g g g s g g g g s
 CAA GGG ACC CTG GTC ACC gtc tcc tca ggtggaggcggttcaggcggaggtggctct
 BstEII
 g g g g s d i E L T Q T P L S L P V
 ggcggtggcggtcgac atc GAG CTC ACC CAA ACT CCA CTC TCC CTG CCT GTC
 SacI
 S L G D Q A S I S C R S S Q S I
 AGT CTT GGA GAT CAA GCC TCC ATC TCT TGC AGA TCT AGT CAG AGC ATT
 V H S N G N T Y L E W Y L Q K P
 GTA CAT AGT AAT GGA AAC ACC TAT TTA GAA TGG TAC CTG CAG AAA CCA
 PstI
 G Q S P K L L I Y K V S N R F S
 GGC CAG TCT CCA AAG CTC CTG ATC TAC AAA GTT TCC AAC CGA TTT TCT
 G V P D R F S G S G S G T D F T
 GGG GTC CCA GAC AGG TTC AGT GGC AGT GGA TCG GGG ACA GAT TTC ACA
 L K I S R V E A E D L G V Y Y C
 CTC AAG ATC AGC AGA GTG GAG GCT GAG GAT CTG GGA GTT TAT TAC TGC
 F Q G S H V P Y T F G G G T K L
 TTT CAA GGT TCA CAT GTT CCG TAC ACG TTC GGA GGG GGG ACC AAG CTC
 E I K R
GAG ATC AAA CGG (SEQ ID NO. 190)
 XhoI (SEQ ID NO. 191)

Fig.14.

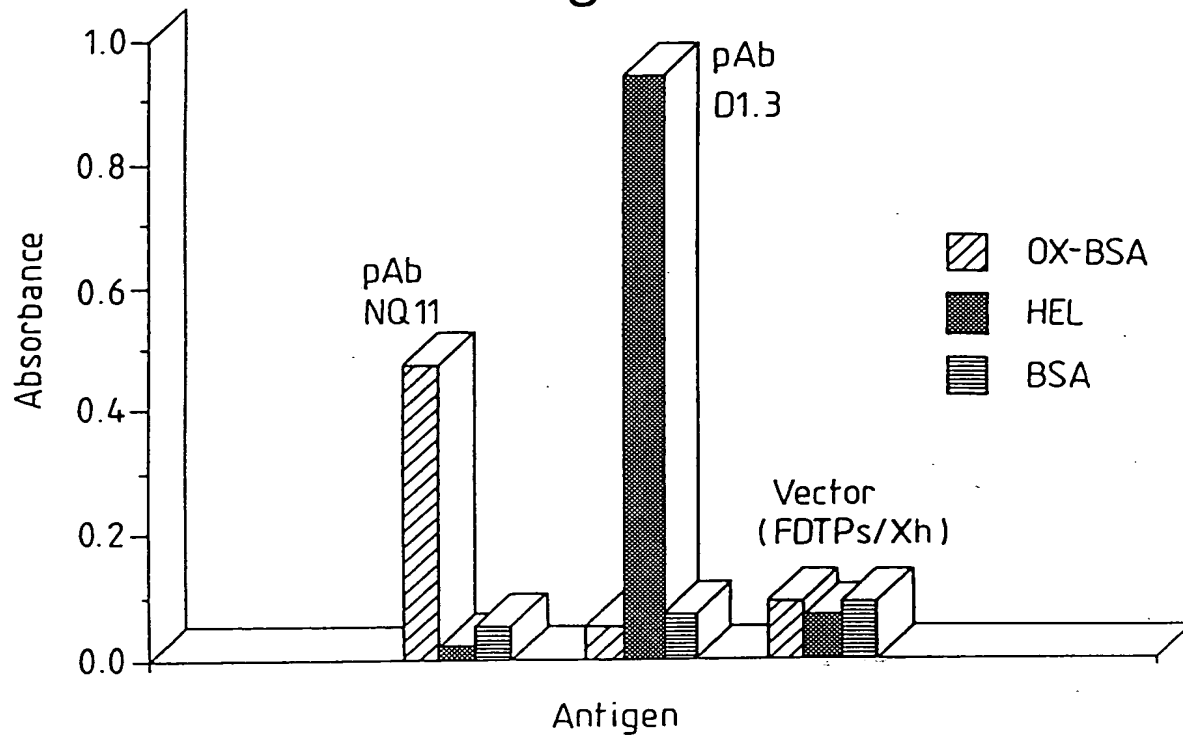


Fig.15.

5' END

TCT CAC AGT GCA CAA ACT GTT GAA CGG ACA CCA GAA ATG CCT GTT CTG (SEQ ID NO:192)
 (SEQ ID NO:193)
 ApaL1

3' END

K A A L G L K
 AAA GCC GCT CTG GGG CTG AAA GCG GCC GCA GAA ACT GTT GAA AGT etc. (SEQ ID NO:194)
 (SEQ ID NO:195)
 Not I

Fig.16a

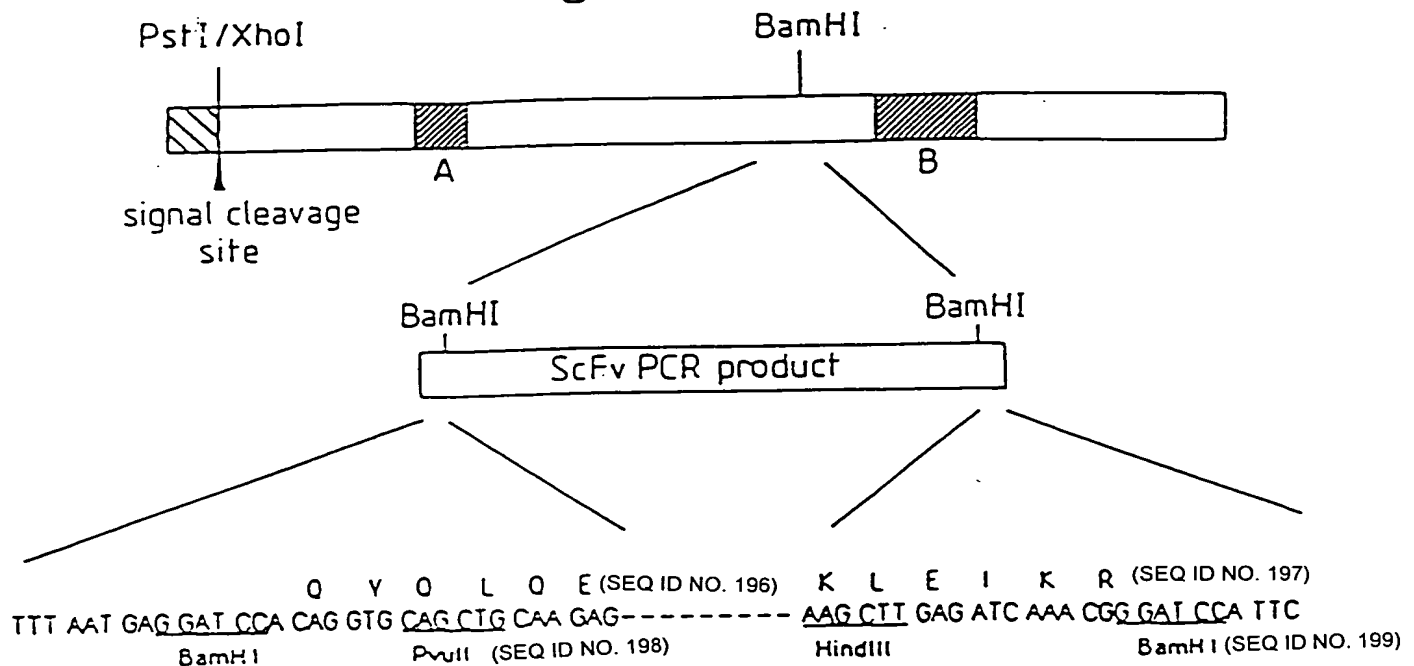
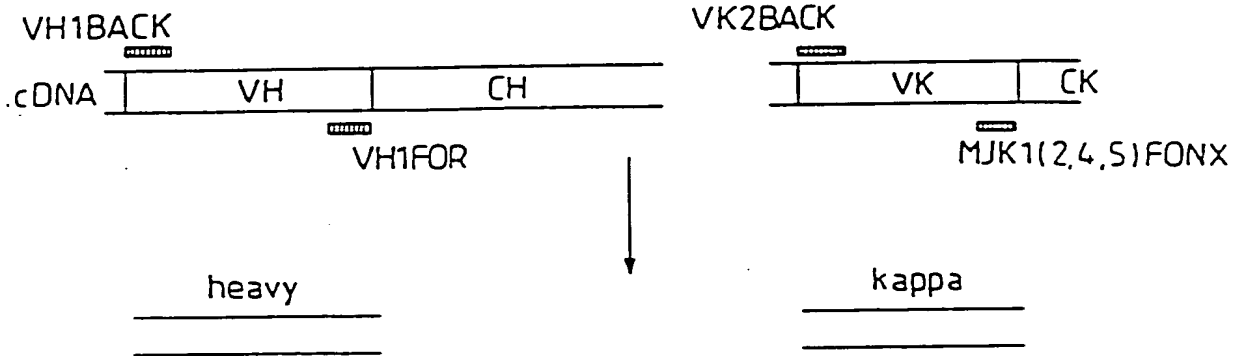


Fig.16b

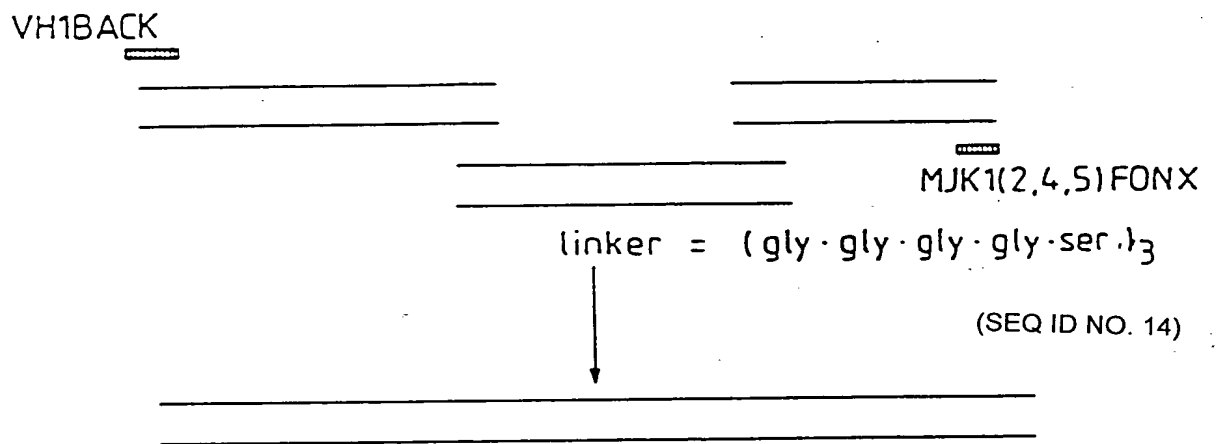
A	(1834)	5'	GAG GGT GGT GGC TCT	(SEQ ID NO. 200)
		-	- - °C - -	(SEQ ID NO. 201)
		-	- - °C - -	(SEQ ID NO. 202)
		-	- - °C - ACT 3'(1839)	(SEQ ID NO. 203)
B	(2284)	5'	GGC GGC GGC TCT	(SEQ ID NO. 204)
		-	GGT GGT GGT -	(SEQ ID NO. 205)
		-	- GGC GGC -	(SEQ ID NO. 206)
		GAG	- - GGC -	(SEQ ID NO. 207)
		-	- - GGT -	(SEQ ID NO. 208)
		-	- - GGC -	(SEQ ID NO. 209)
		-	- - GGT -	(SEQ ID NO. 210)
		-	- - GGC - 3'(2379)	(SEQ ID NO. 211)
Reverse complement of mutagenic oligo G3Bamlink				
		5'	GAG GGT GGC GGA TCC	(SEQ ID NO. 212)
			GAG GGT GGC GG 3'	(SEQ ID NO. 213)

Fig.17.

1) PRIMARY PCR



2) ASSEMBLY PCR



3) ADDING RESTRICTION SITES

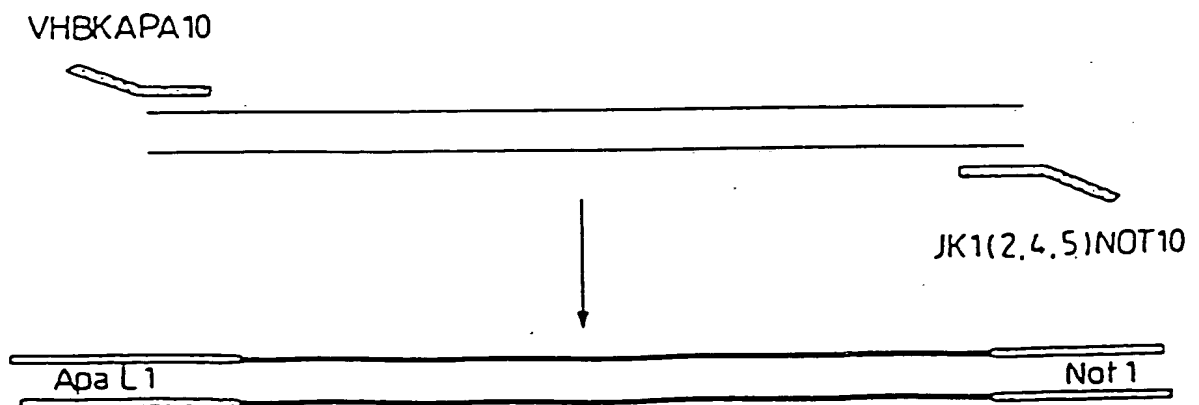


Fig.18.

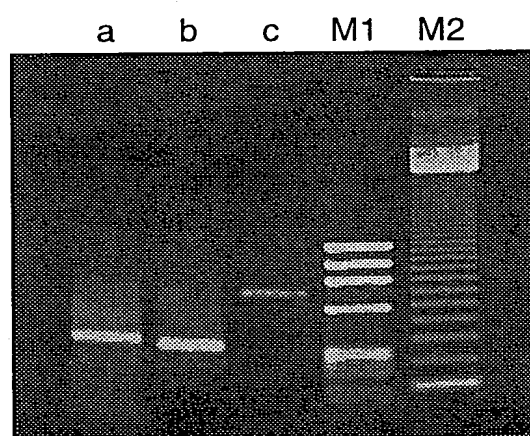


Fig.19.

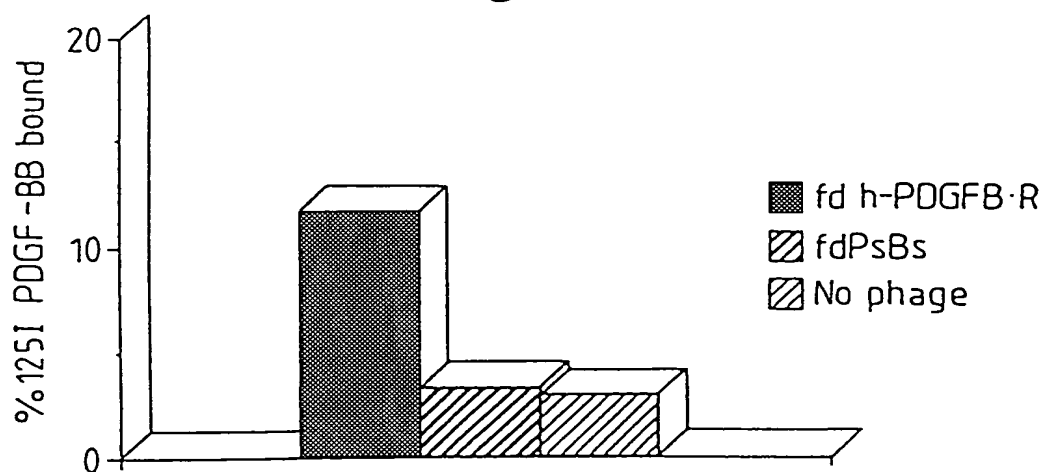


Fig.20.

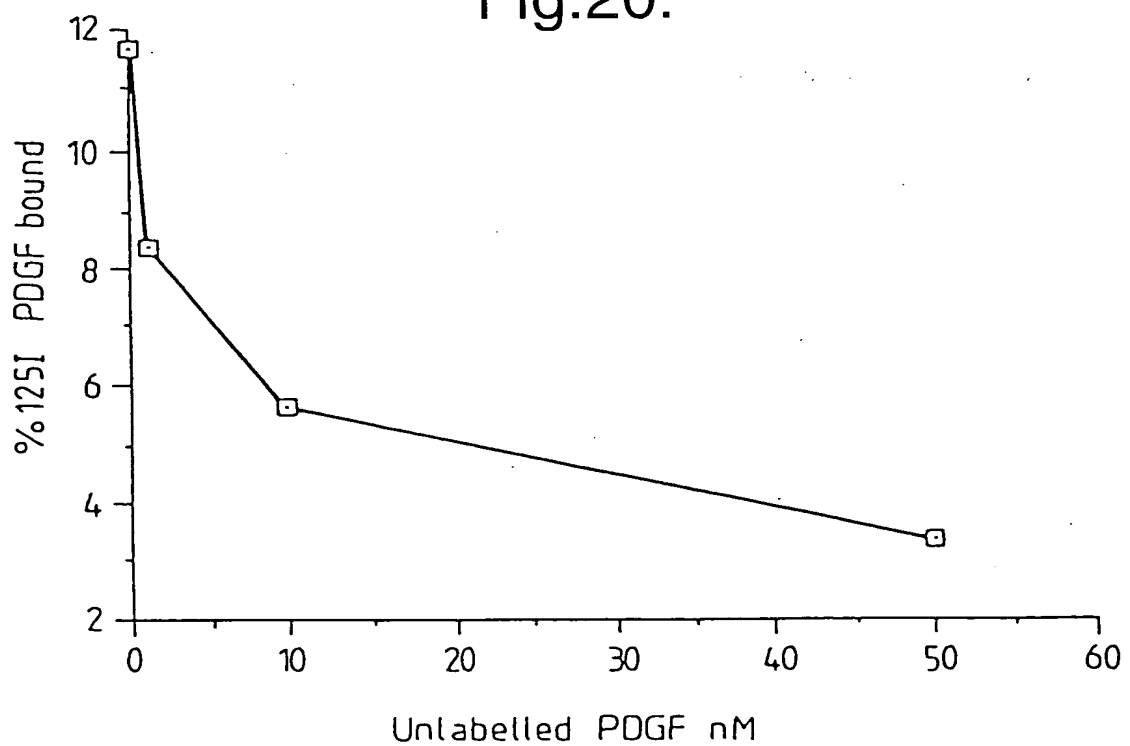


Fig.21.

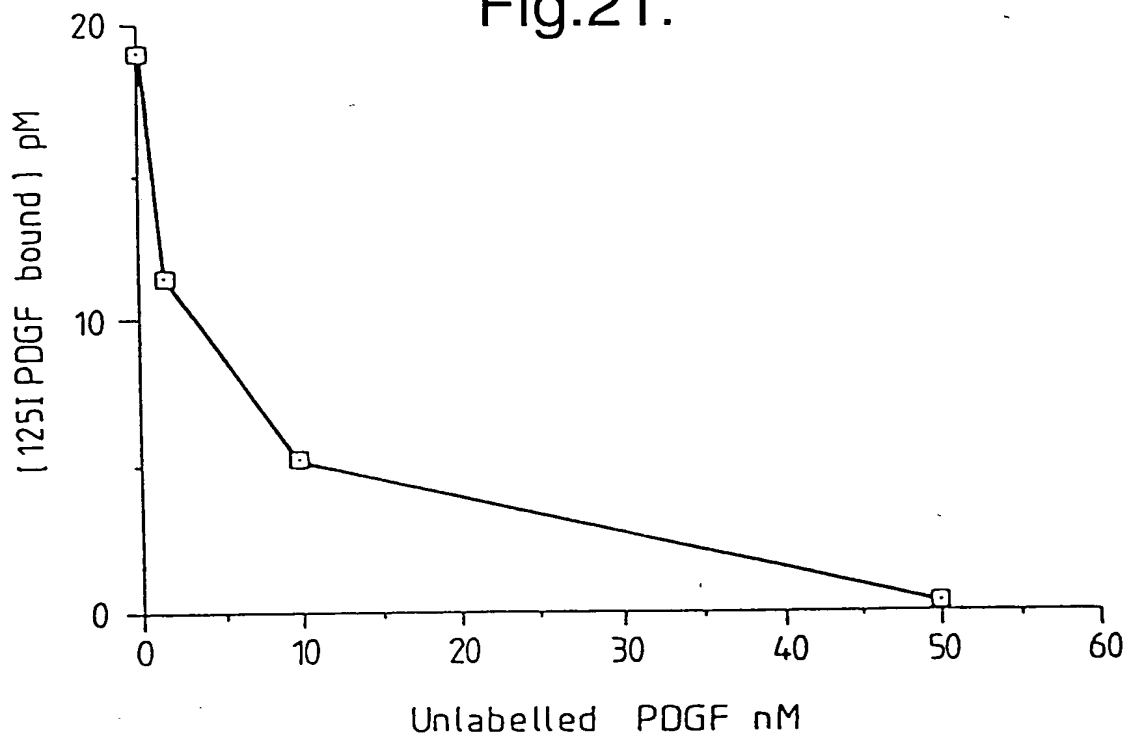


Fig.22.

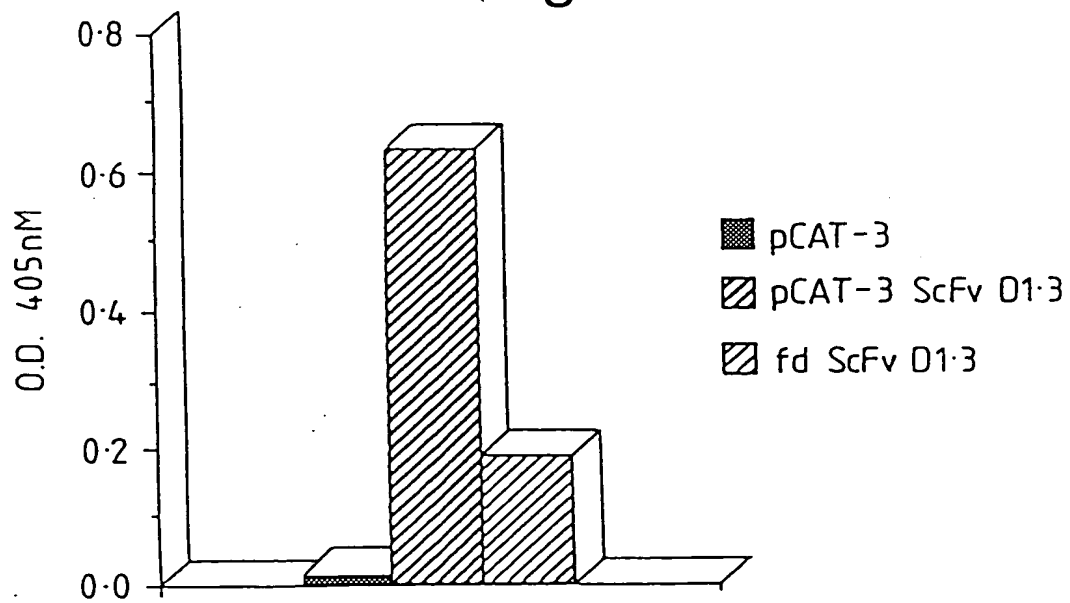


Fig.23a

d
M

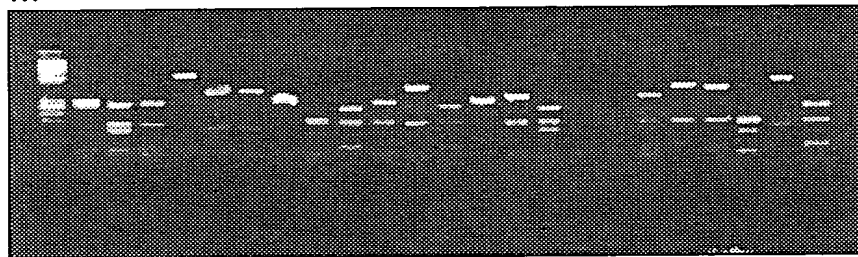
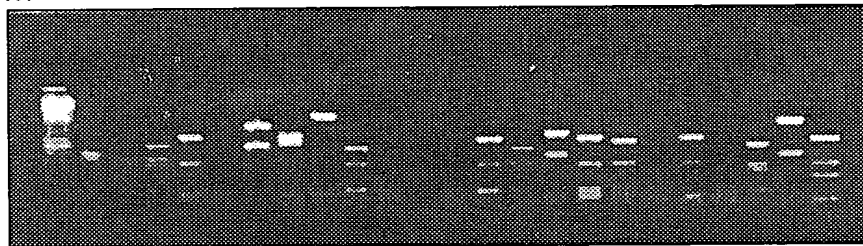


Fig.23b

M



VH sequences

Fig.24a

from combinatorial library:

	CDR1		CDR2		CDR3		
A	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 214)
B	QVQLQQS0AELAKPGAGVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 215)
C	QVQLQQS0P ELVXPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 216)
D	QVQLQQS0P ELVXPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 217)
E	QVQLQQS0P ELVXPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 218)
F	QVQLQQS0P ELVXPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 219)
G	QVQLQQS0AELVXPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 220)
H	QVQLQQS0P ELVXPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 221)

from hierarchical library VH-rep x Vc-d:

I	QVQLQQS0P ELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 222)
J	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 223)
K	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 224)
L	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 225)
M	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 226)
N	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 227)
O	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 228)
P	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 229)
Q	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 230)
R	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 231)
S	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 232)
T	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 233)
U	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 234)
V	QVQLQQS0AELARPGASVXHSCKASGYTFT	WVKQRPQCGLEWIG	YINPSSGYTNYNQKFKD	KATLTADKSSSTAYHQLSSLTSEDSAVTYCAH	RYGAY	WQGGTTVTVS9	(SEQ ID NO. 235)

Fig.24b

V κ sequences

from combinatorial library:

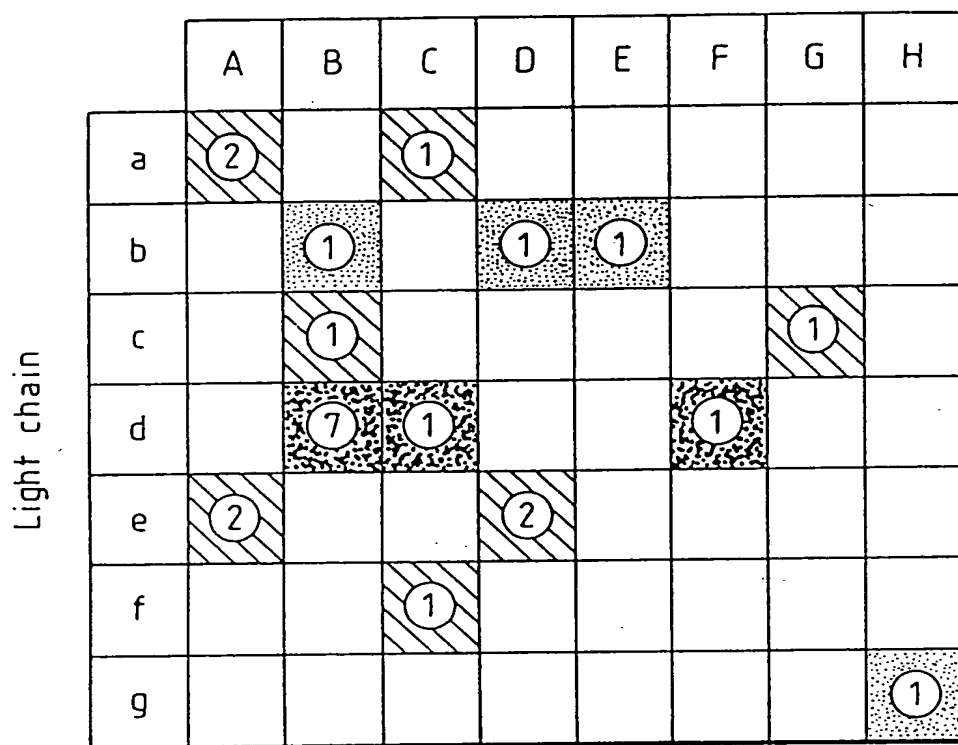
	CDR1	CDR2	CDR3		
a	DIELTQSPSSLSASLCERVELTC	WLOQKPDGSIKRLIY	AASLTLES	GVPAKFSGSRSGSDYSLTISSEEDFADYTC	LOYASYPT
b	DIELTQSPAIHSAASPCVKVHTC	WYQKSGCASPVMIIY	BTSHLAS	GVPAKFSGSGGTGYSLTISSEVEDAATYYC	QQYSGTPLT
c	DIELTQSPPTTHAASPGCKITITC	WYQKPGFSPKLLIY	RTSHLAS	GVPAKFSGSGSGTSYSLTICTHEAEDVATYYC	QQGSSIPLT
d	DIELTQSPPTTHAASPGCKITITC	WYQKPGFSPKLLIS	RTSHLAS	GVPAKFSGSGSGTSYSLTICTHEAEDVATYYC	QQGSTIPFT
e	DIELTQSPAIHSAASPGCKVITC	WYQKPGTSPKLMIIY	STSHLAS	GVPTKFSGSGSGTSYSLTISRHEAEDAATYYC	QQRSYPPT
f	DIELTQSPATHSAFPGCKVHTC	WYQKSGTSPKRMIIY	DTSKLAS	GVPAKFSGSGSGTSYSLTISSEAEDAATYYC	QQFSNPILT
g	DIELTQSPAIHSAASPGCKVHTC	WYQKPGCASPVMIIY	DTSKLAS	GVPAKFSGSGSGTSYSLTISSEHAEADAATYYC	IQRNSYPHT

from hierarchical library VH-B x V κ -rep:

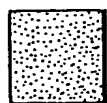
h	DIELTQSPAIHSAASPGCKVHTC	SASSSVSTYDI	DTSKLAS	GVPAKFSGSGSGTSYSLTISSEHAEADAATYYC	QQM6SNPLT	FGACTKLEIKRA	x4	IV/VI	V κ ox1	(SEQ ID NO. 243)
i	DIELTQSPAIHSAASPGCKVHTC	SASSSV6YIH	STSHLAS	GVPAKFSGSGSGTSYSLTISRHEAEDAATYYC	QQYHSYPLT	FGACTKLEIKRA	x4	V	ox-1like?	(SEQ ID NO. 244)
j	DIELTQSPPTTHAASPGCKITITC	SASS91SSNYLH	RTSHLAS	GVPAKFSGSGSGTSYSLTICTHEAEDVATYYC	QQGSSIPLT	FGGTTKLEIKRA	x4	V	ox-1like	(SEQ ID NO. 245)
k	DIELTQSPPTTHAASPGDHITITC	SATS61SSNYLH	RTSHLAS	GVPPKFSGSGSGTSYSLTICTHEAEDVATYYC	QQG89IPYT	FGACTKLEIKRA	x4	V	ox-1like	(SEQ ID NO. 246)
l	DIELTQSPPTTHAASPGCKITITC	SASS91SSNYLH	RTSHLAS	GVPAKFSGSGSGTSYSLTICTHEAEDVATYYC	QQGSGIPYT	FGGTTKLEIKRA	x4	V	ox-1like	(SEQ ID NO. 247)
m	DIELTQSPPTTHAASPGCKITITC	SASS91SSNYLH	RTSHLAS	GVPAKFSGSGSGTSYSLTICTHEAEDVATYYC	QQG6GIPYT	FGGTTKLEIKRA	x4	V	ox-1like	(SEQ ID NO. 248)
n	DIELTQSPPTTHAASPGCKITITC	6AS61SSNYLH	RTSHLAS	GVPAKFSGSGSGTSYSLTICTHEAEDVATYYC	QQGSSIPFT	FGGTTKLEIKRA	x4	V	ox-1like	(SEQ ID NO. 249)
o	DIELTQSPAIHSAASPGCKITITC	SA6961SSNYLH	RTSHLAS	GVPAKFSGSGSGTSYSLTICTHEAEDVATYYC	QQG89IPYT	FGGTTKLEIKRA	x4	V	ox-1like	(SEQ ID NO. 250)
p	DIELTQSPAIHSAASPGCKVHTC	SASSSVSTYDI	DTSKLAS	GVPAKFSGSGSGTSYSLTISRHEAEDAATYYC	QQM6SNPLT	FGACTKLEIKRA	x4	IV/VI	V κ ox1	(SEQ ID NO. 251)
q	DIELTQSPAIHSAASPGCKVHTC	6ASSVRYVN	DTSKLAS	GVPAKFSGSGSGTSYSLTISRHEAEDAATYYC	QQM7SNPPT	FGGTTKLEIKRA	x4	IV/VI	V κ ox1	(SEQ ID NO. 252)
r	DIELTQSPAIHSAASPGCKVHTC	6ASSSV6YIH	DTSKLAS	GVPAKFSGSGSGTSYSLTISRHEAEDAATYYC	QQM5TNALT	FGACTKLEIKRA	x4	IV/VI	V κ ox1	(SEQ ID NO. 253)
s	DIELTQSPAIHSAASPGCKVHTC	RA65SVT58YLN	STSHLAS	GVPAKFSGSGSGTSYSLTISRHEAEDAATYYC	QQYSGYPLT	FGACTKLEIKRA	x4	IV/VI	ox-1like	(SEQ ID NO. 254)
t	DIELTQSPAIHSAASPGCKVHTC	RA65SV96SYLN	STSHLAS	GVPAKFSGSGSGTSYSLTISRHEAEDAATYYC	QQRSYPLT	FGACTKLEIKRA	x4	IV/VI	ox-1like	(SEQ ID NO. 255)
u	DIELTQSPAIHSAASPGCKVHTC	RA65SV56SYLN	STSHLAS	GVPAKFSGSGSGTSYSLTISRHEAEDAATYYC	QQY6GYPLT	FGACTKLEIKRA	x4	IV/VI	ox-1like	(SEQ ID NO. 256)
v	DIELTQSPAIHSAASPGCKVHTC	RA65SV566YLN	STSHLAS	GVPAKFSGSGSGTSYSLTISRHEAEDAATYYC	QQYSGYPLT	FGGTTKLEIKRA	x4	IV/VI	ox-1like	(SEQ ID NO. 257)
w	DIELTQSPPTTHAASPGCKITITC	SASS91SSNYLH	RTSHLAS	GVPAKFSGSGSGTSYSLTICTHEAEDVATYYC	QQGSGIPLT	FGACTKLEIKRA	x4	IV/VI	ox-1like	(SEQ ID NO. 258)

Fig.25.

HEAVY CHAIN



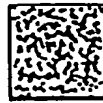
OD_{405nm} in ELISA



0.2-0.9



0.9-2.0



>2.0

Fig.26(a).

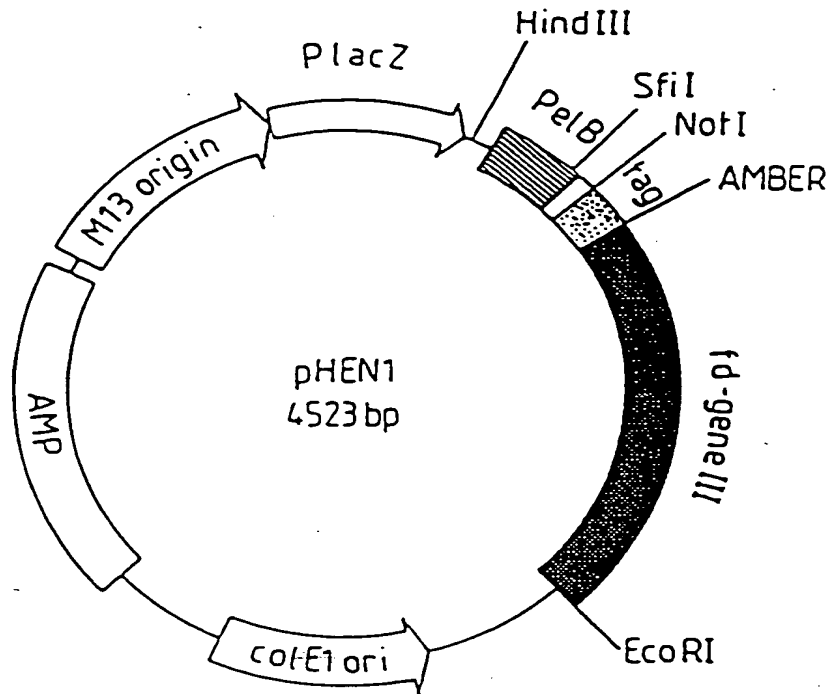


Fig.26(b).

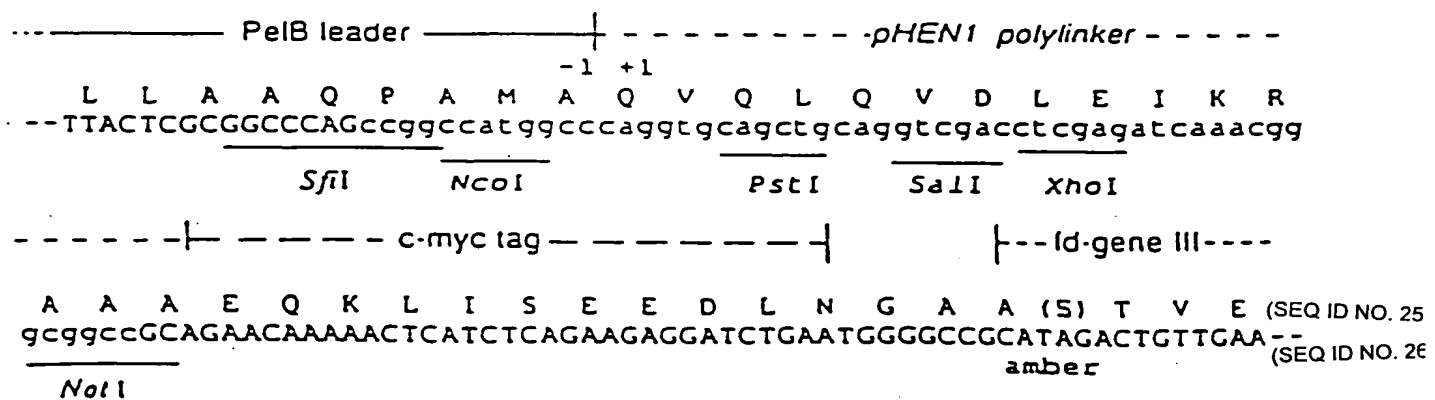


Fig.27.

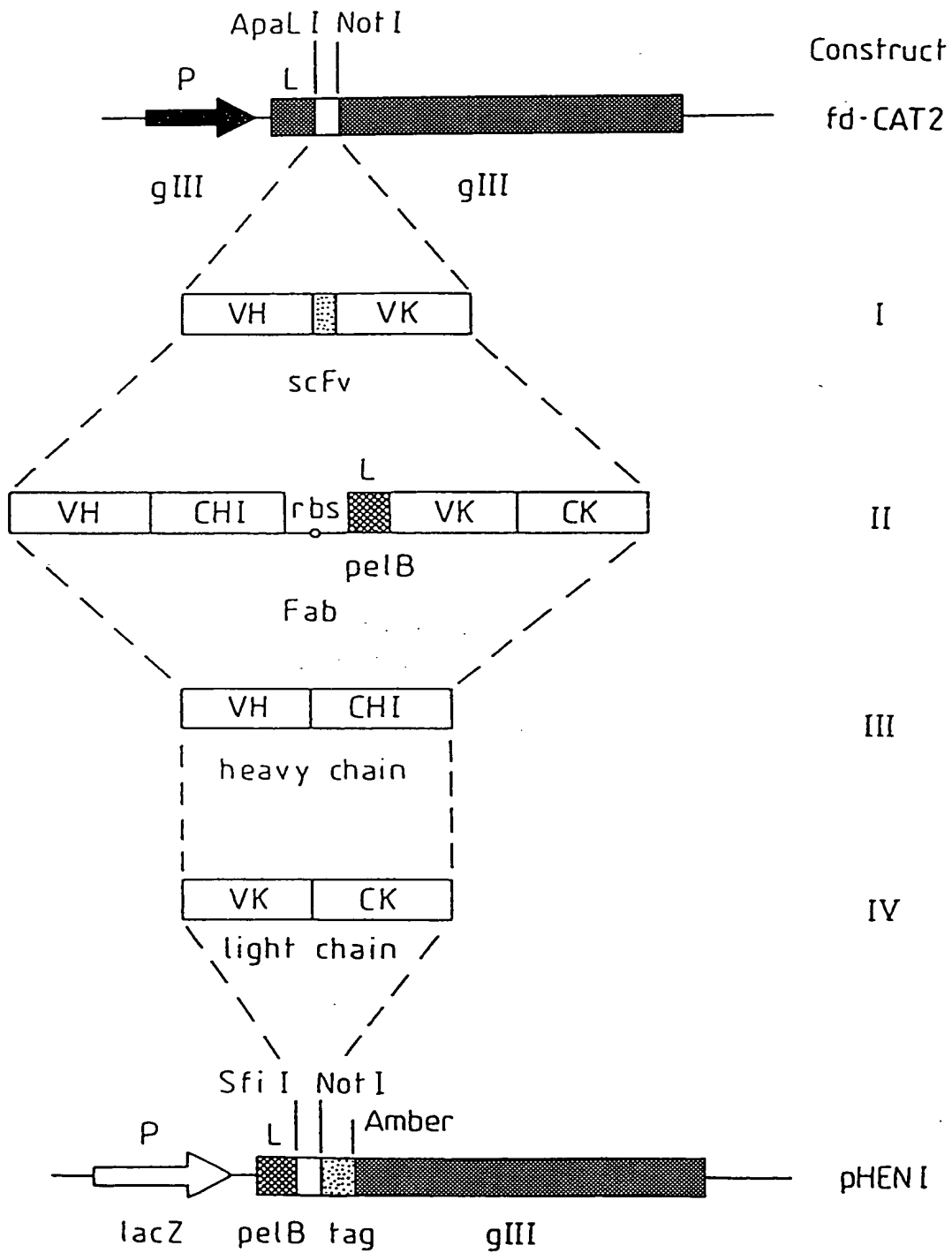


Fig.28.

Fab

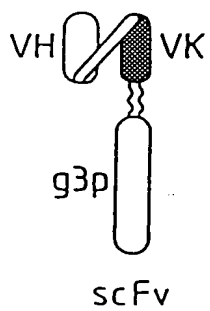
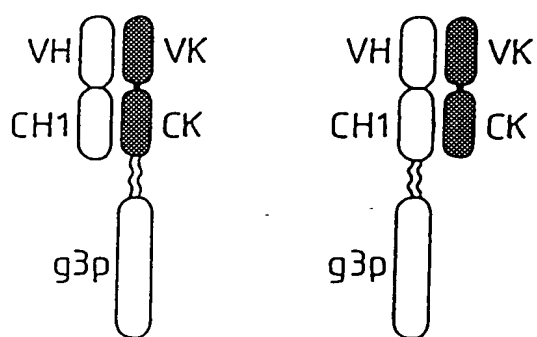


Fig.29.

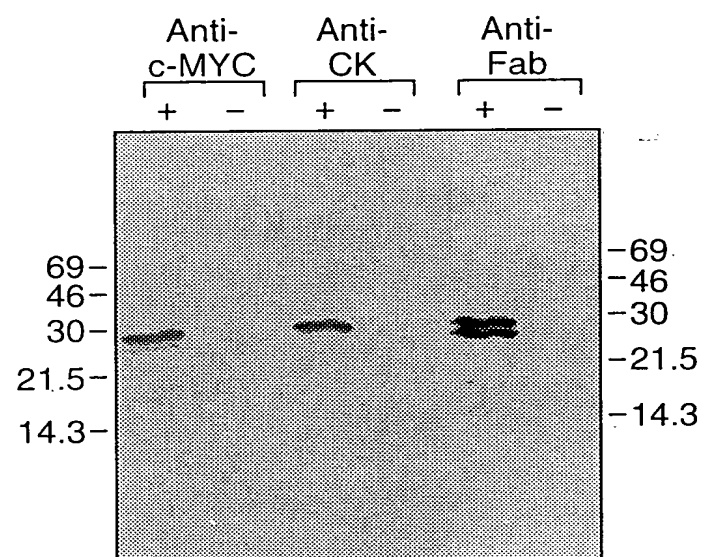


Fig.30.

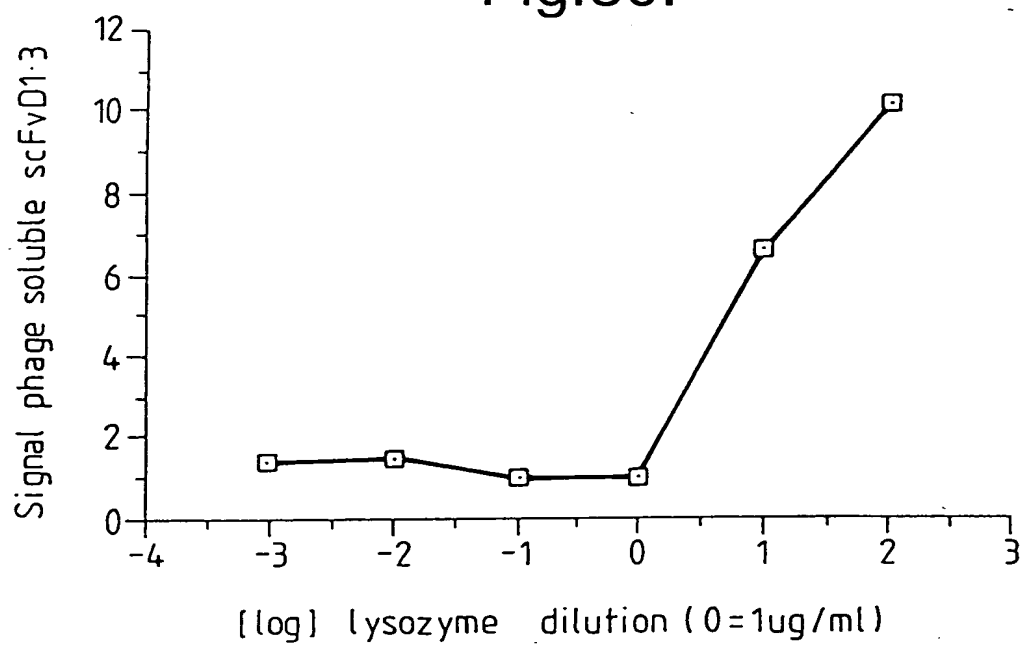


Fig.31.

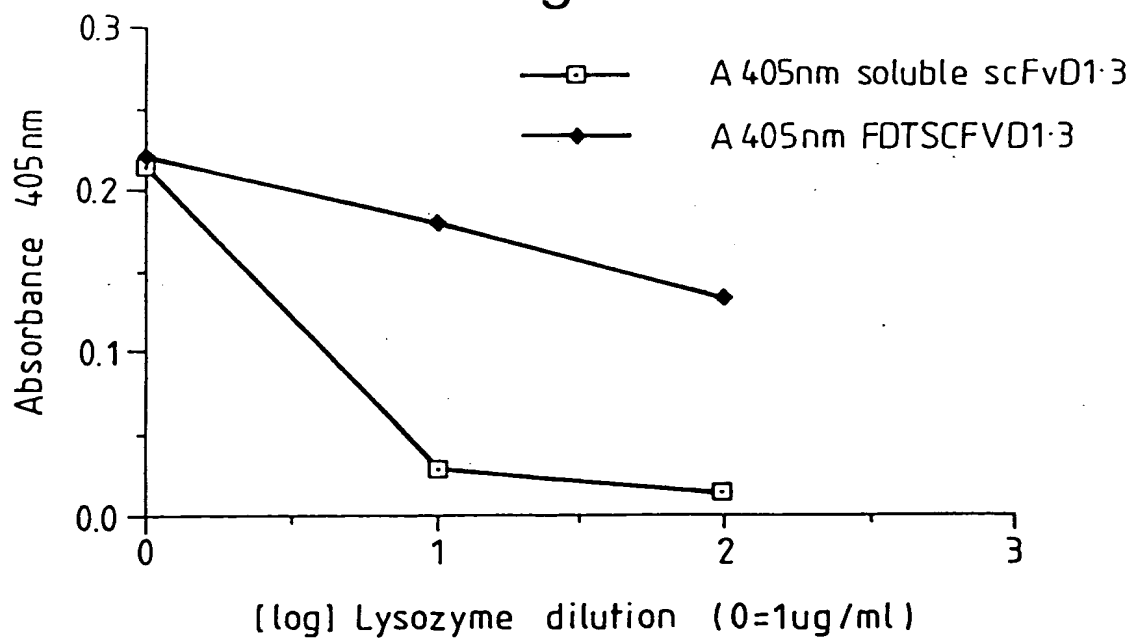


Fig.32.

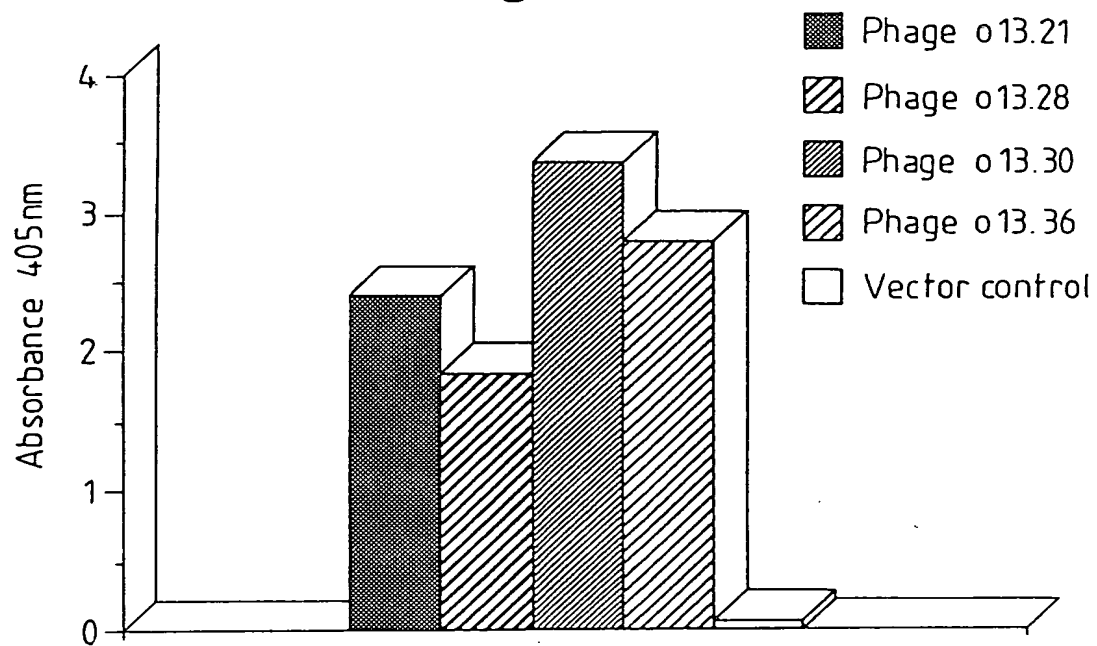


Fig.33.

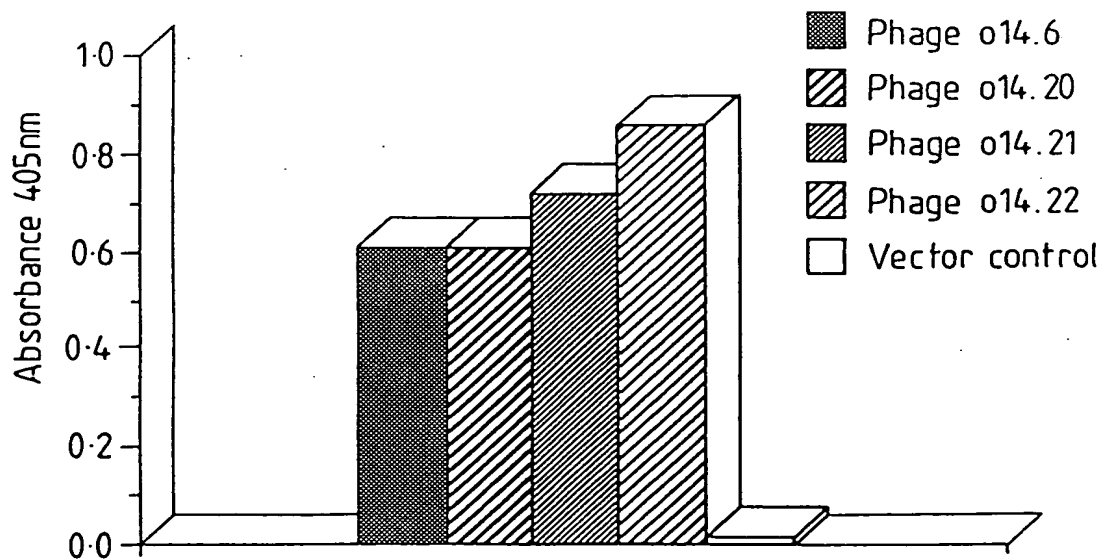


Fig.34.

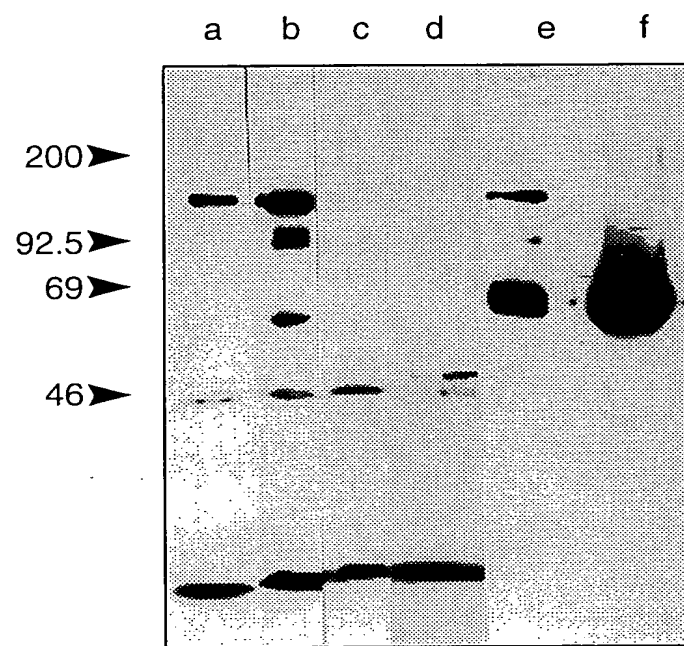


Fig.35A.

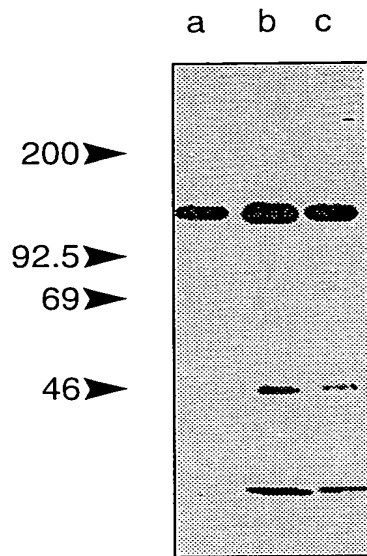


Fig.35B.

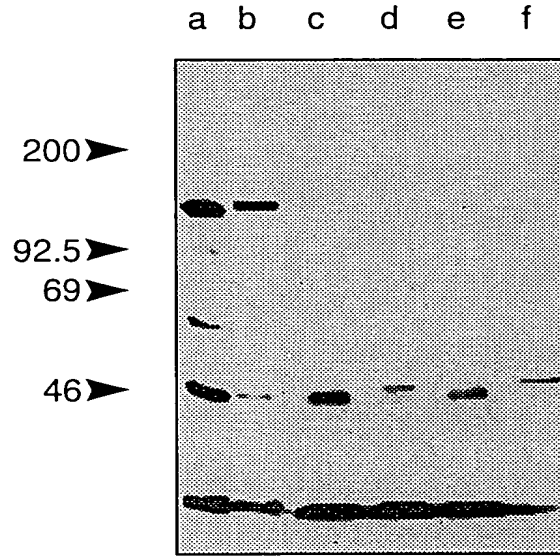


Fig.36.

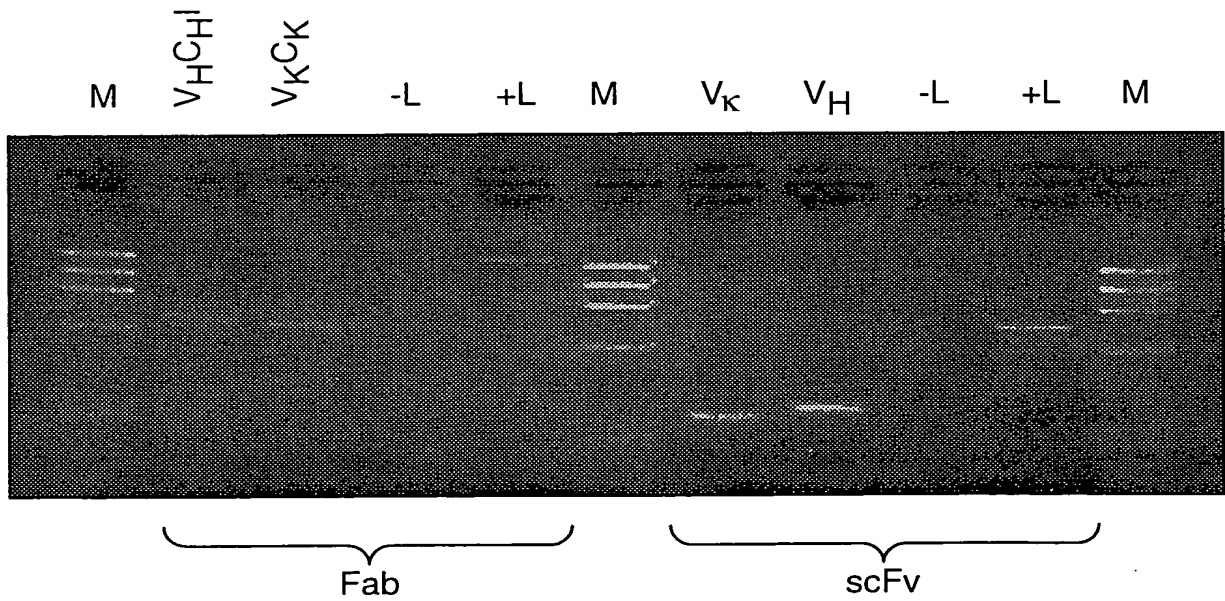


Fig.37.

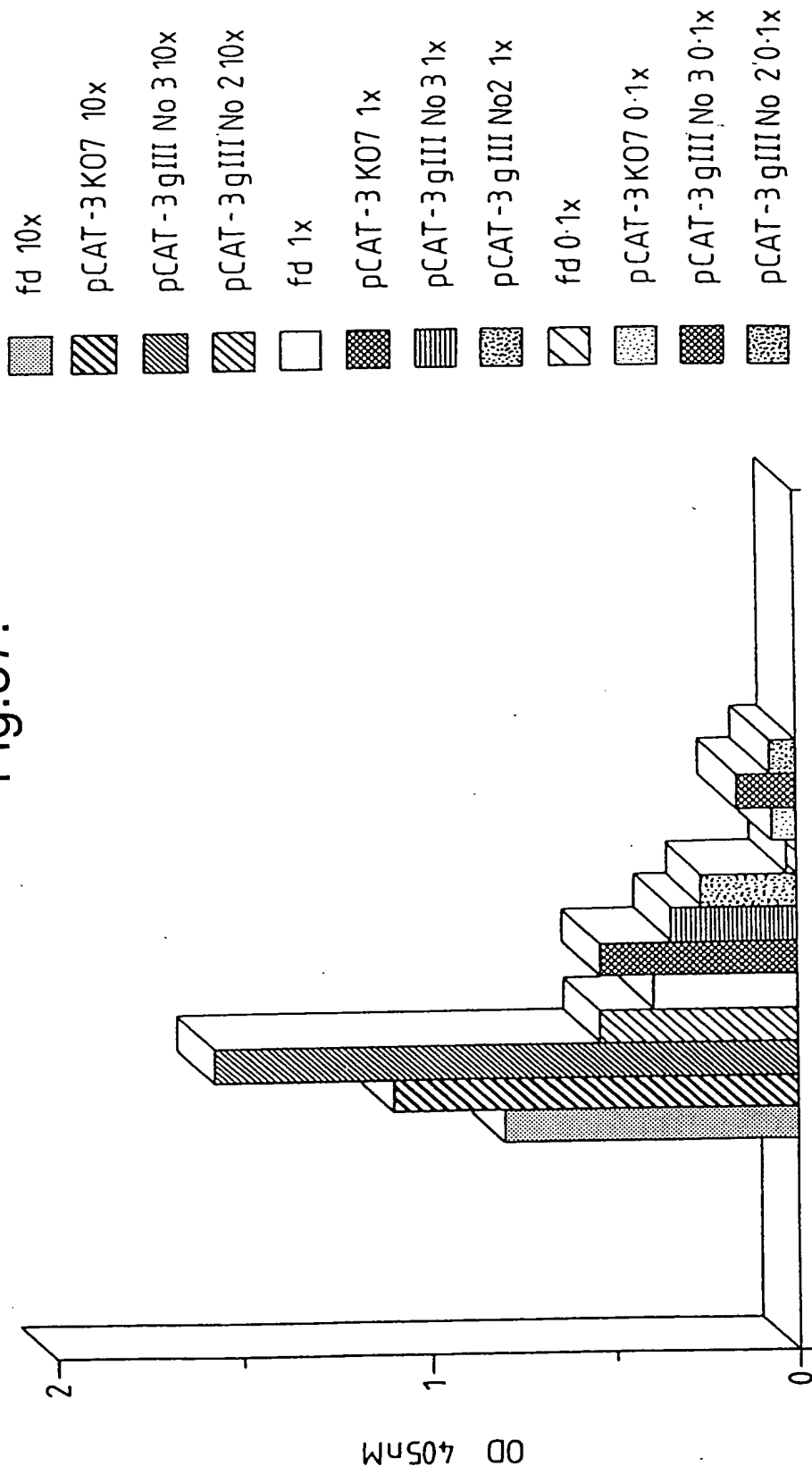


Fig.38A.

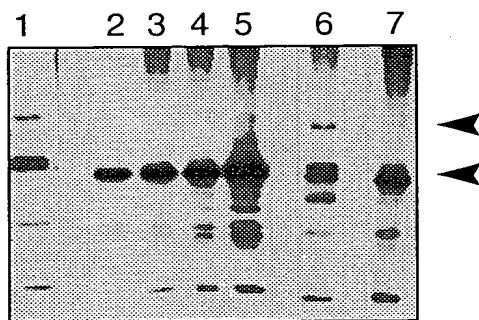


Fig.38B.

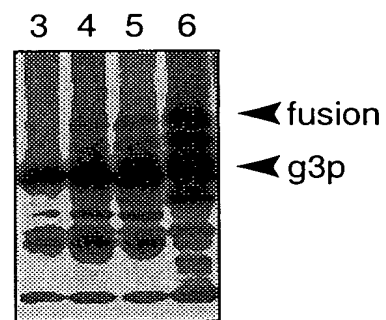


Fig.39.

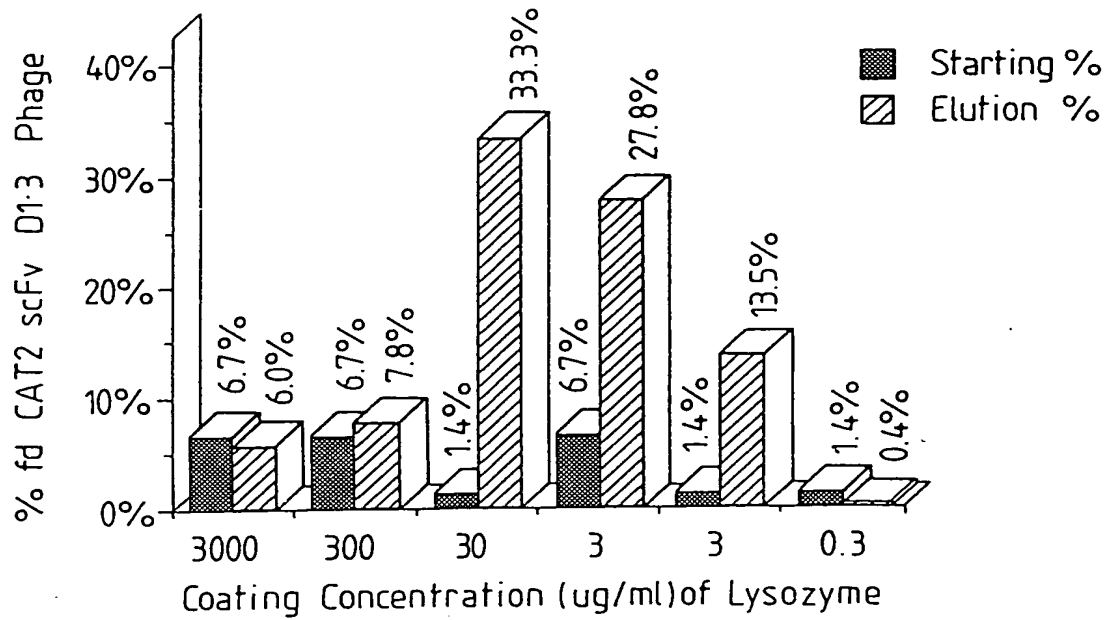


Fig.40.

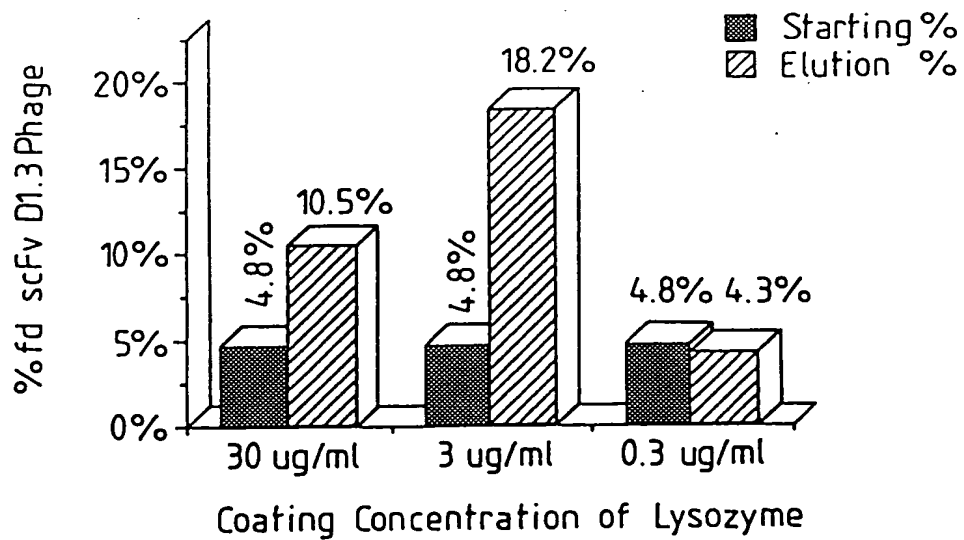


Fig.41.

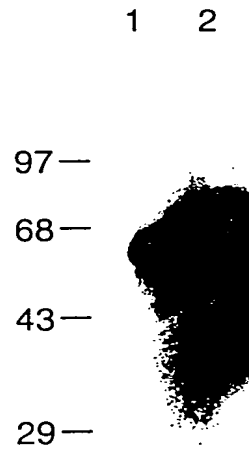


Fig.42.

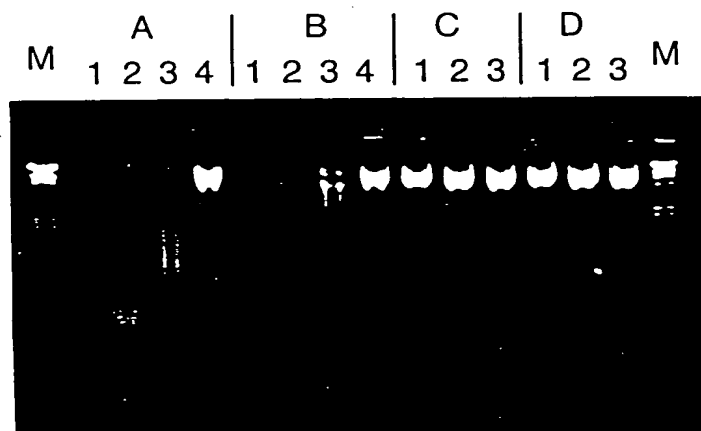


Fig.43.

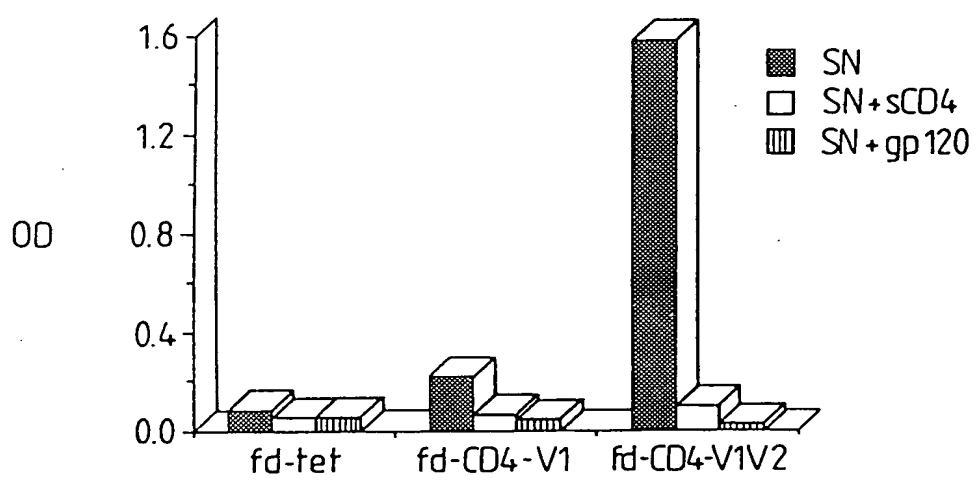


Fig.44a

10	20	30	40	50	60	70	80	90
TTCTATTCTCACAGTGCAAGGTCCAGCTGCAGCAGTCTGGGGCTGAGCTTGTGAAGCCTGGGGCTTCAAGTGAAGCTGTCTCCTGCAAGGCT								
AAGATAAGAGTGTACCGTGTCCAGGTCGATCGTCAGACCCCGACTCGAACACTTCGGACCCCGAAGTCACTTCGACAGGACGTTCCCGA								
PheTyrSerHisSerAlaGlnValGlnLeuGlnSerGlyAlaGluLeuValLysProGlyAlaSerValLysLeuSerCysLysAla								
100	110	120	130	140	150	160	170	180
TCTGGCTACACCTTCACAGCTACTGGATGCACCTGGGTGAAGCAGAGGCCCTGGACGAGGCCTTGAGTGGATTGGAAGGATTGATCCTAAT								
AGACCCGATGTGGAAGTGGTCGATGACCTACGTGACCCACTTCGTCTCCGGACCTGCTCCGGAACCTCACCTAACCTTCCCTAACTAGGATTA								
SerGlyTyrThrPheThrSerTyrTrpMetHisTrpValLysGlnArgProGlyArgGlyLeuGluTrpIleGlyArgIleAspProAsn								
190	200	210	220	230	240	250	260	270
AGTGGTGGTACTAAGTACAATGAGAAGTTCAAGAGCAAGGCCACACTGACTGTAGACAAACCCCTCCAGCACAGCCCTACATGCAGCTCAGC								
TCACCACCATGATTCAATGTTACTCTTCAAGTCTCGTTCGGGTGACTGACATCTGTCTTGGAGGTCGTGTGGATGTACGTCGAGTCG								
SerGlyGlyThrLysTyrAsnGluLysPheLysSerLysAlaThrLeuThrValAspLysProSerSerThrAlaTyrMetGlnLeuSer								
280	290	300	310	320	330	340	350	360
AGCCTGACATCTGAGGACTCTGCGGTCTATTATTGTGCAAGATACGACTACGGTAGTAGCTACTACTTTGACTACTGGGGCCAAAGGACC								
TCGGACTGTAGACTCCTGAGACGCCAGATAATAACACGTTCTATGTGTATGCCATCATCGATGATGAACACTGATGACCCCGGTTCCCTGG								
SerLeuThrSerGluAspSerAlaValTyrTyrCysAlaArgTyrAspTyrGlySerSerTyrTyrPheAspTyrTrpGlyGlnGlyThr								
370	380	390	400	410	420	430	440	450
ACGGTCACCGTCTCCTCAGGTGGAGGCGGTTTCAGGCGGAGGTGGCTCTGGCGGTGGCGGATCCAGGCTGTTGGGACACAGGAATCTGCA								
TGCCAGTGGCAGAGGATCCACCTCCGCCAAGTCCGCCCTCCACCGAGACCGCCACCGCCTAGGTCGGACAAACCCTGTGTCTTAGACGT								
ThrValThrValSerSerGlyGlyGlySerGlyGlyGlySerGlyGlyGlySerGlnAlaValGlyThrGlnGluSerAla								
460	470	480	490	500	510	520	530	540
CTCACACATCACCTGGTGAACACAGTCACACTCACTTGTTCGCTCAAGTACTGGGGCTGTTACAACTAGTAACATATGCCAACTGGGTCCAA								
GAGTGGTGTAGTGGACCACTTTGTCAAGTGTAGTGAACAGCGAGTTCATGACCCCGACAAATGTTGATCATTTGATACGGTTGACCCAGGTT								
LeuThrThrSerProGlyGluThrValThrLeuThrCysArgSerSerThrGlyAlaValThrThrSerAsnTyrAlaAsnTrpValGln								
550	560	570	580	590	600	610	620	630
GAAAAACAGATCATTTATTACCTGGTCTAATAGGTGTACCAACAACCGAGCTCCAGGTGTTCTCTGCCAGATTCTCAGGCTCCCTGATT								
CTTTTGGTCTAGTAAATAAGTGACCCAGATTATCCACCATTGTTGCTCGAGGTCCACAAAGGACCGTCTAGAGTCCGAGGGACTAA								
GluLysProAspHisLeuPheThrGlyLeuIleGlyGlyThrAsnAsnArgAlaProGlyValProAlaArgPheSerGlySerLeuIle								

Fig.44 b

640	650	660	670	680	690	700	C	G	710	720
GGAGACAAGGCTGCCCC	TCACCATCACAGGGGCACAGACTGAGGATGAGGC	AATATATTCTGTGCTCTATGG	AC	AGCAACCAATTGGGTG						
CCTCTGTTCCGACGGGAGTGGTAGTGTCCCCCGTGTCTGACTCCTACTCCGTTATATAAGACACGAGATACCATGTCTGTTGGTAACCCAC										
GlyAspLysAlaAlaLeuThrIleThrGlyAlaGlnThrGluAspGluAlaIleTyrPheCysAlaLeuTrpTyrnberAsnHisTrpVal										
730	740	750	760	770						
TTC	GTGGAGGA	CAAACTGACTGTCCCTCGAGATCAAAACGGGGCGCGC			(SEQ ID NO. 261)					
AAGCCACCTCCTTGGTTGACTGACAGGAGCTCTAGTTGCCCGCGCGCG										
PheGlyGlyGlyThrLysLeuThrValLeuGluIleLysArgAlaAla					(SEQ ID NO. 262)					

Fig.45.

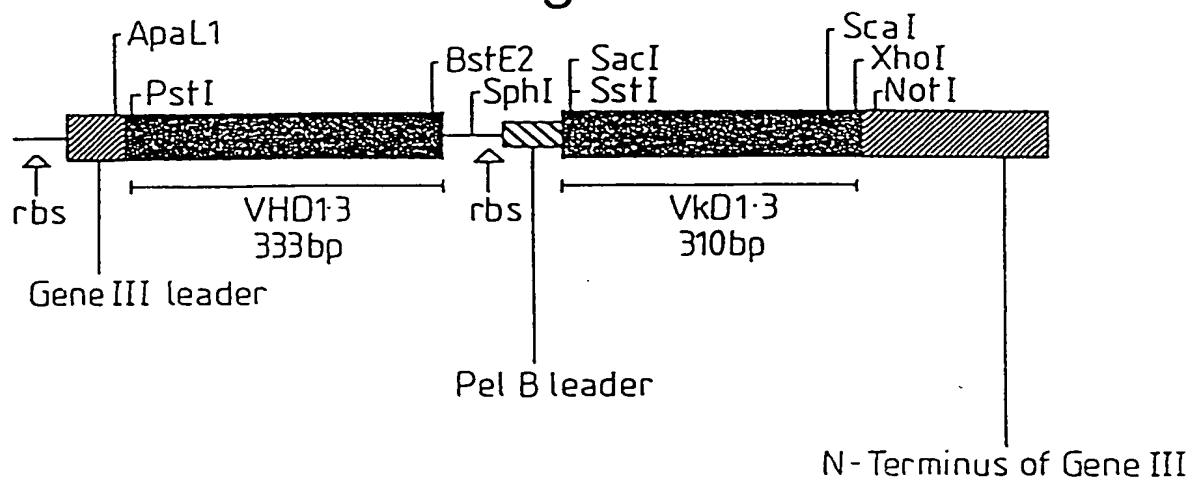


Fig.46.

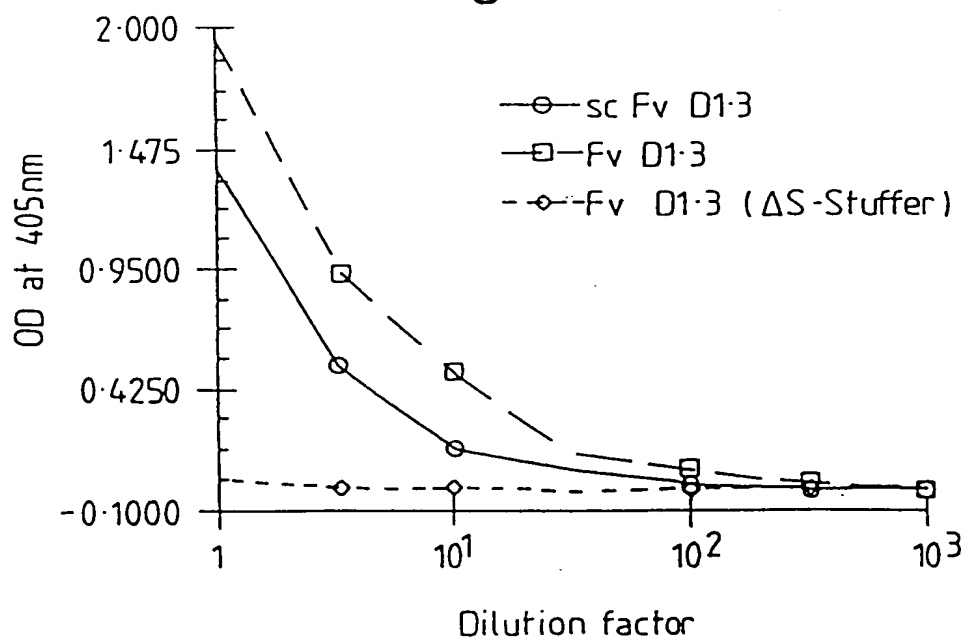


Fig.47.

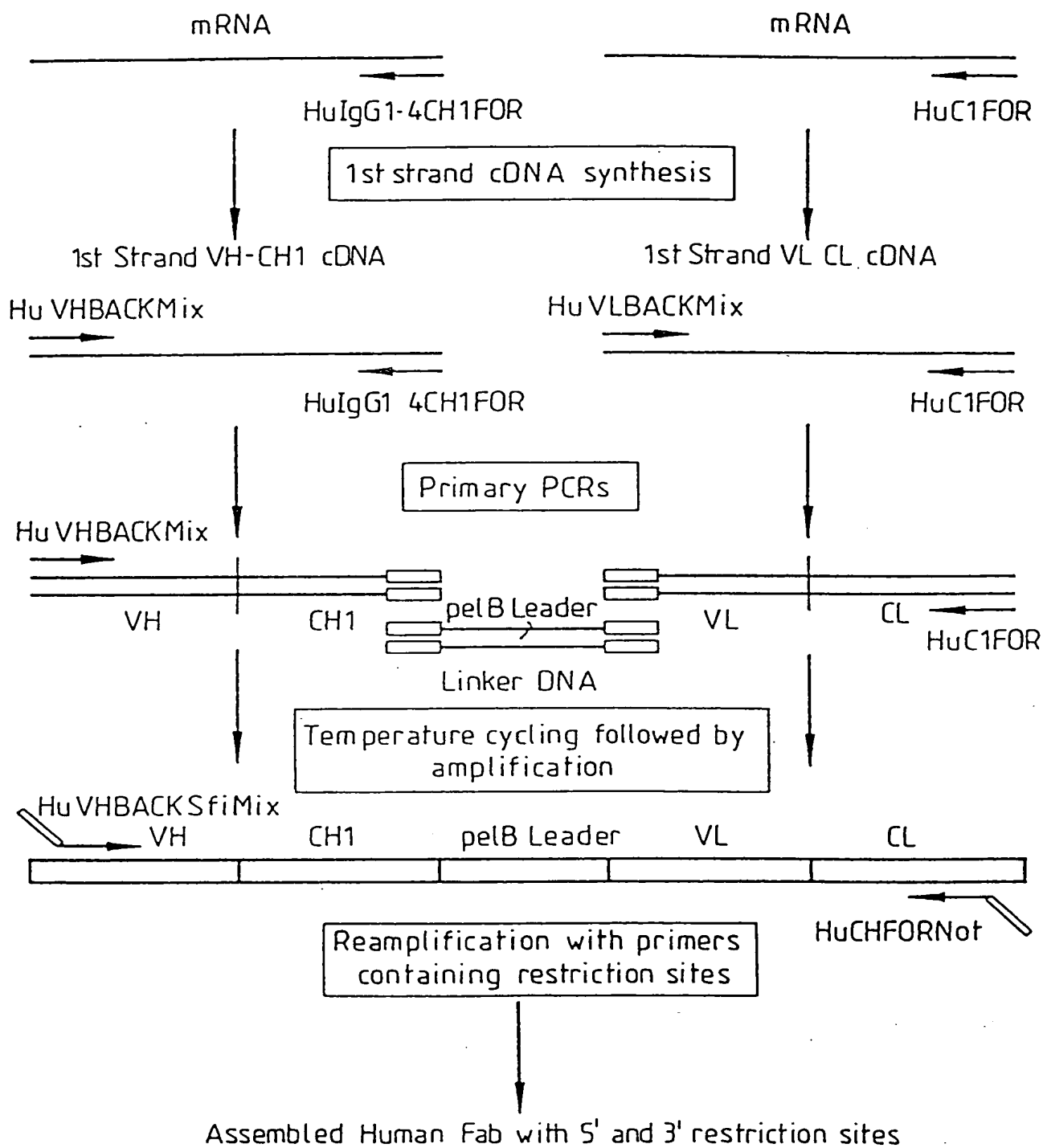


Fig. 48a

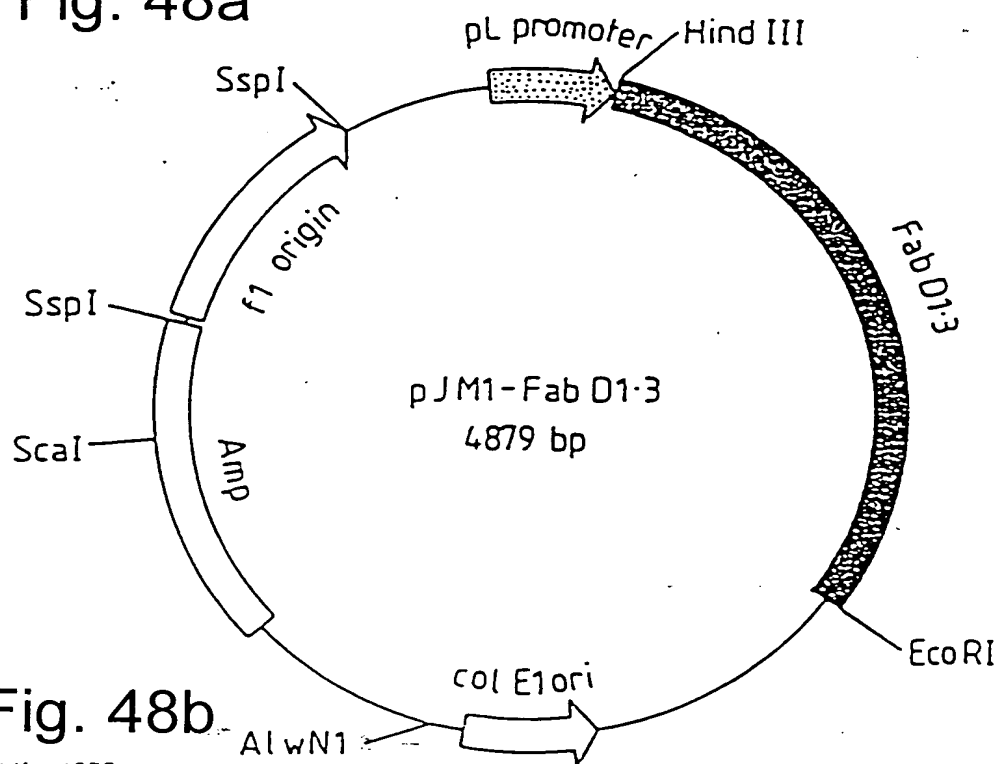


Fig. 48b

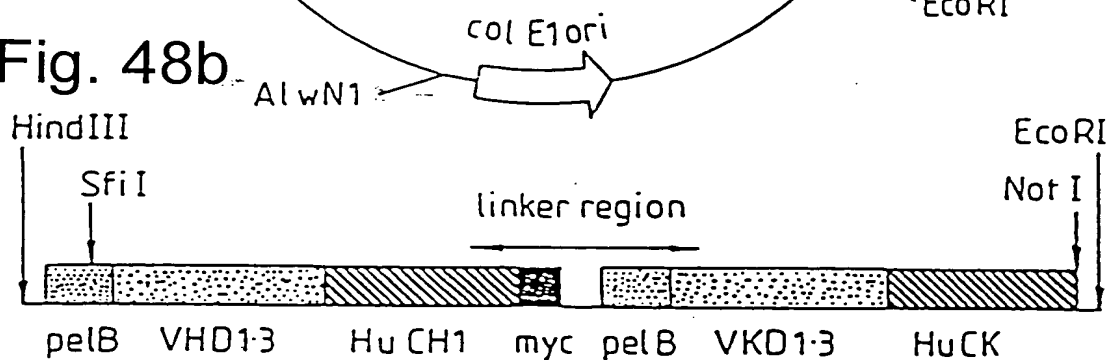


Fig. 48c

← 3' Human CH1 and hinge →
K P S N T K V D K K V E P K S S T K T H T
A A C C C C A G C A A C A C C A A G G T C G A C A A G A A G T T G A G C C C A A T C T T C A A C T A A G A C G C A C A C A

→ myc peptide tag →
S G G E Q K L I S E E D L N * *
T C A G G A G G T G A C A G A A G C T C A T C T C A G A A G A G G A T C T G A A T T A A T A A G G G A G C T T G C A T G C A

(SEQ ID NO. 263)

← pelB leader →
M K Y L L P T A A A G L
A A T T C T A T T T C A A G G A G A C A G T C A T A T G A A T A C C T A T T G C C T A C G G C A G C C G C T G G A T T G T

→ 5' Vk →
L L P A A Q P A M A D I E L T Q S P
T A T T A C C T G C T G C C C A A C C A G C G A T G G C C G A C A T G A G T T C A C C C A G T C T C C

(SEQ ID NO. 264)
(SEQ ID NO. 265)

Fig.49.

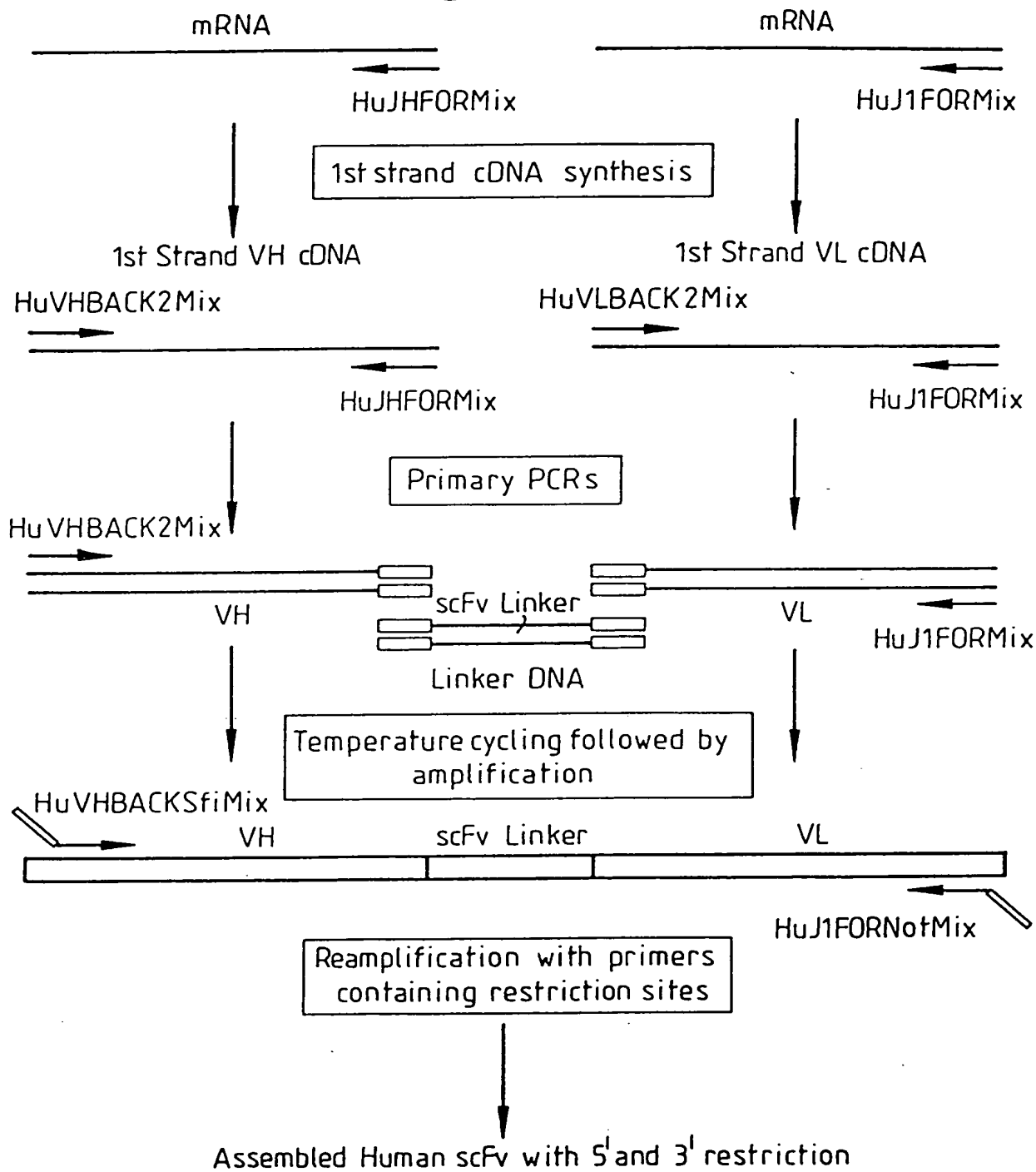


Fig.50a

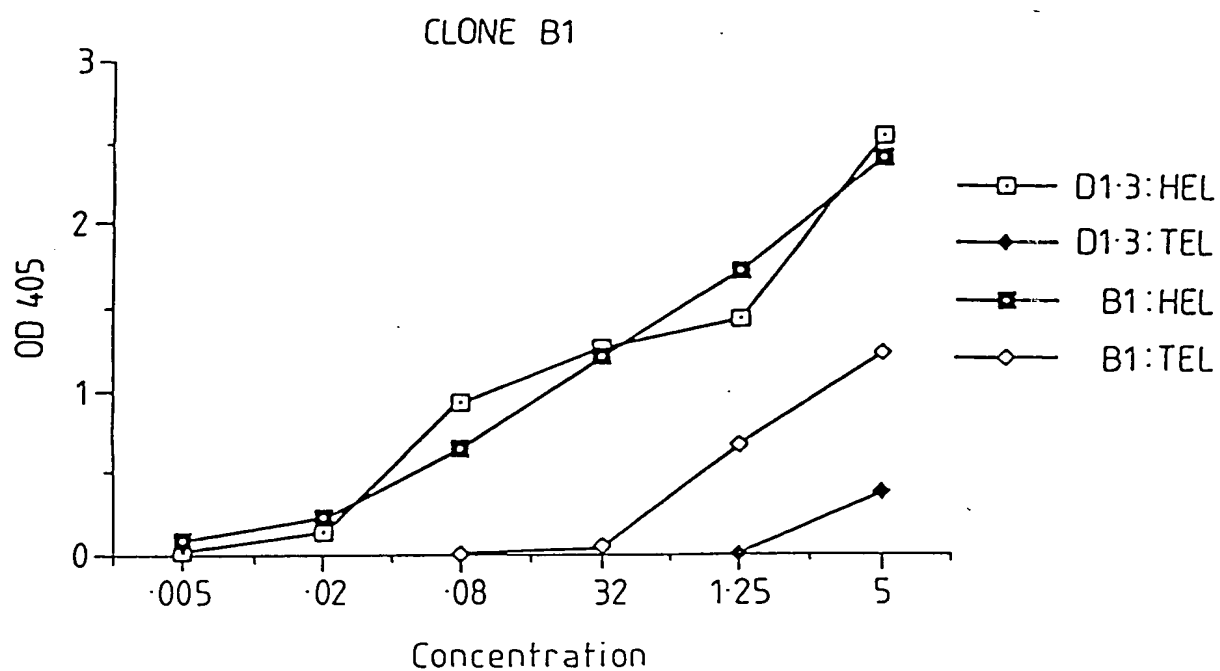


Fig.50b

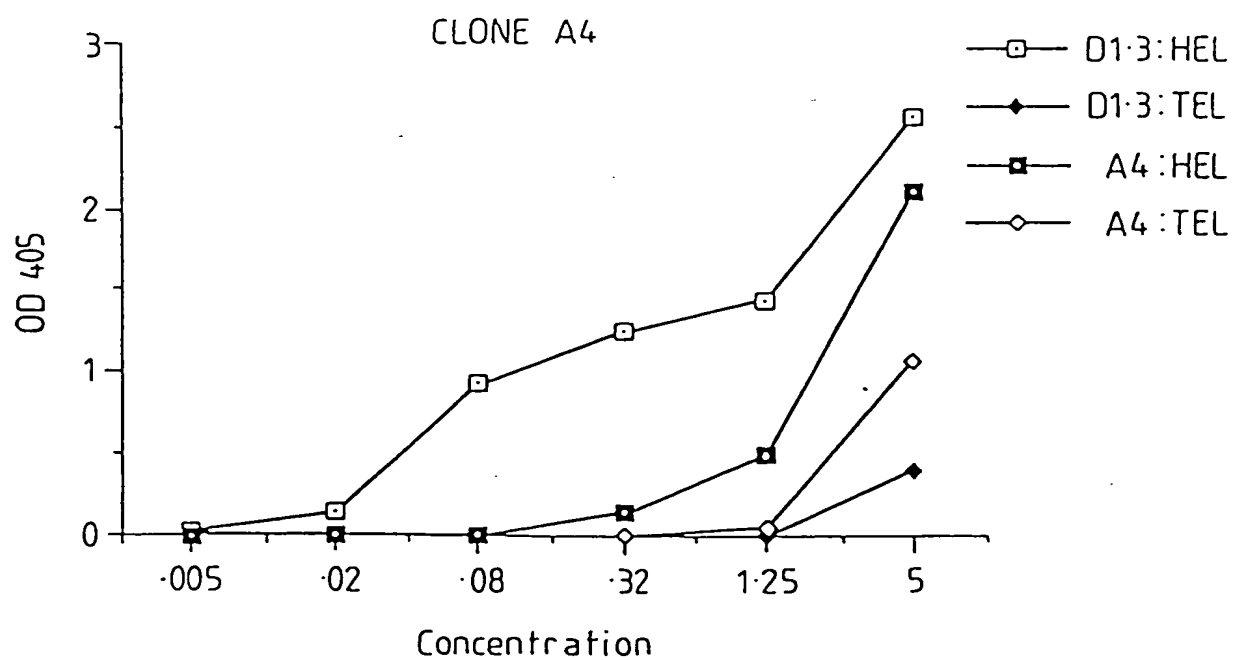


Fig.51.

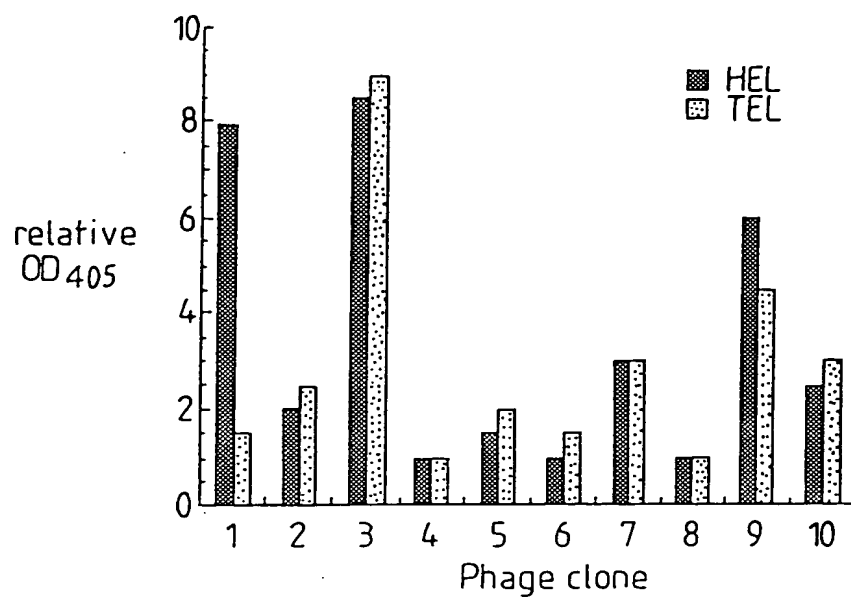


Fig.53.

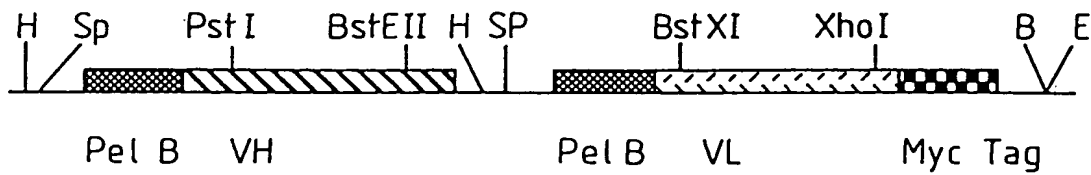


Fig.52.

	CDR 1	CDR 2
D1.3	DIQMTQSPASLSASVGETVTITCRASGNIHNYLA	WYQQKQKGKSPQLLVYYTTLAD
M1F	DIELTQSPSSLSASLGERVSLTCRASQDIGSSLN	WLQQEPDGTIKRLIYATSSLDS
M21	DIELTQSPALMAASPGEKVTITCSVSSSISSSNLHWYQQKSETSPKPKWIYGTSNLAS	

	CDR 3
D1.3	GVPSRFSGSGGTQYSLKINSLQPEDFGSYQCQHFWSPTPRTFGGGTKLEIKR
M1F	GVPKRFGSRSGSDYSLTISSESEDFVDYYCLQYASSPWTFGGGTKLELKR
M21	GVVPRFSGSGGTSYSLTISSEAEADAATYYCQQWSSYPPLTFGAGTKLEIKR